Acid Deposition Research Program

THE SOUTHWESTERN ALBERTA MEDICAL DIAGNOSTIC REVIEW

Volume One

METHODOLOGY

DESIGNED AND EXECUTED BY:
THE McGILL INTER-UNIVERSITY RESEARCH GROUP

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VOLUME I - - METHODS

by
McGill Interuniversity Research Group
with
the Epidemiology Rapid Response Unit
of the Montreal General Hospital

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Note

This is the final report of the MDR. In the interests of providing the public with the report at the time of the community meetings, and because of the compressed time frames involved in report production, some typographical or arithmetical errors may exist. Further exhaustive editing is in progress.

The definitive version eliminating any such production errors will be printed by the fall of 1986.

CREDIT AND RESPONSIBILITY

The completion of this Medical Diagnostic Review in Southwestern Alberta and the preparation of this final report in one year is a tribute to the teams of men and women in the inter-university research group co-ordinated by McGill University and our colleagues associated with the Acid Deposition Research Program (ADRP).

The co-investigators and professionals listed in the next pages have earned most of the credit for the timeliness and the quality of this study. Having benefitted from the wise counsel of many senior peers and my staff the responsibility for the conclusions published and for any errors is mine alone.

This document, in two volumes and several technical appendices, has been submitted to The Honourable Mr. James F. Dinning, Minister of Community and Occupational Health and to the Co-Chairmen of the ADRP at Edmonton on June 9, 1986.

My colleagues and I thank the government and the citizens of Alberta for the trust placed in us in helping resolve with them one of the most challenging Canadian problems at the interface of the environment and the health of the public.

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Southwest Alberta Medical Diagnostic Review

Montreal, June 9, 1986

June, 1986

SOUTHWEST ALBERTA MEDICAL DIAGNOSTIC REVIEW PROJECT

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McGill Interuniversity Research Group
with the Epidemiology Rapid Response Unit
of the Montreal General Hospital

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The Southwest Alberta Medical Diagnostic Review Project was funded by the Department of Community and Occupational Health of Alberta and administered by the Acid Deposition Research Program.

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DEFINITIONS AND FREQUENTLY USED TERMS

ADRP - Acid Deposition Research Program.

A priori - Refers to statements or assumptions or statistical criteria set forth in advance of commencing the field work of the Medical Diagnostic Review Project (MDR); the converse of this term in the report is either post-hoc or a posteriori.

Algorithms - A step-by-step procedure for solving a problem or accomplishing some end; in the clinical context this refers to classification methods or treatment decisions done by pre-determined ground rules.

Biostatistics - Quantitative methods of analysing information about living creatures.

CAB - Community Advisory Boards.

CHS - Canada Health Survey: data is from 1978-79 Statistics Canada Health Survey and figures quoted are for all of Canada except when specified.

Cardinal clinical outcome - The symptoms, signs and diagnoses that are most plausibly associated with the environmental risk factors of concern in the Index Areas.

Clinical epidemiology - The study of determinants and effects of clinical decisions.

Clinical significance - A difference sufficiently great that it is impressive because of its consequences for the health of people; clinical significance takes into account the unavoidable reality of uncontrollable or unforeseeable biases as well as real but trivial differences; clinical significance is referred to as "delta" by many statisticians and in every day language it could be referred to as "the difference that makes a difference".

Clustering - The phenomenon of "bunching-up" of people or events or diagnoses; clustering could be in relation to time (for instance there may be an unusual number of cases of measles within a three-month period in a given location), it could be in relation to geography (there might be an unexpectedly high number of cases of absenteeism from school in one village as compared to surrounding ones); clustering could be in relation to diagnosis itself (even though total mortality due to heart disease might be the same in two areas, one could note a clustering of many cases of heart attack in one community versus another).

Cohort - A group of persons sharing common characteristics at a given point in time and defined by an event such as birth, admission to hospital or residence in a particular location.

Corroborate - In the context of this report, corroboration occurs when in comparisons of DCCI versus SR-M the direction of the difference and the magnitude of the difference observed is similar to differences noted in the comparison of IA versus SR.

DCCI - Didsbury - Carstairs - Crossfield - Irricana, exposed control area, north of Calgary.

Demography - The statistical study of human populations especially with reference to size and density, distribution and vital statistics.

Epidemiology - The study of determinants of health and disease in human populations; it includes the study of incidence, distribution and control of disease in a population.

Etiology - Cause or the study of cause.

Heavy (or trace) metals - Metals found in the environment that could penetrate a person's system to dangerous or toxic levels.

IA - Index Area, or the main area of interest exposed to environmental contaminants of concern. An area of southwestern Alberta in and around the towns of Twin Butte, Glenwood, Hill Spring, Willow Creek and Mountain View.

IA (MC) - Index Area outmigrants most comparable to outmigrants from SR and DCCI, consisting only of first degree relatives from the IA outmigrants respondents.

Incidence Period - January 1, 1970 - December 31, 1984

Incident Cancer - Any cancer occurring in a member of the Index Area 1970 cohort during the incidence period as registered by the Alberta Cancer Registry. (Please note: it is recognized under this definition that only cancers that occurred within the Province of Alberta will be registered and thus be considered as incident cancers.)

Index Area 1970 cohort - The collection of all individuals who were alive and resident in the Index Area during the calendar year 1970.

M - Abbreviation for population of Mormon religion.

MDR - Medical Diagnostic Review, being the formal name of this health study.

Methodology - The study of methods.

Period prevalence - The frequency of disease in a population within a span of time. Expressed otherwise, the prevalence of a particular health state or disease in a population of

interest during a period of time. For instance the number of diabetics in Toronto during one year, or two weeks. (This is to be contrasted with point prevalence which is the frequency of the disease at a given instant point in time).

Person Years of Risk - A measure of the population at risk of becoming diseased or dying during a defined period of time.

Post-Hoc Hypotheses - Hypotheses that were not formally put forward at the outset of a study but that are made only after looking at the data.

Power (to detect differences) - A measure of the strength that a study has to detect differences that are real.

Protocol - The plan of a scientific experiment or treatment recorded in writing before initiating the scientific work.

Reference rate - A measure of the frequency of disease or health-related events in a reference or control area.

RFP - "Request for Proposal".

SA - Southern Alberta, south of an east-west line running through Edmonton but excluding the Calgary and Edmonton census metropolitan areas. (In some assessments Lethbridge and Medicine Hat are also excluded.)

SAB - Scientific Advisory Board (appointed by the Acid Deposition Research Program).

SAG - Scientific Advisory Group (appointed by McGill University).

Signs - Observed phenomena in people's bodies as ascertained by professionally trained clinicians (usually physicians). Signs, like symptoms, are indicators of the possibility of disease but are generally considered to be objective findings in clinical research.

Sociodemographic - Attributes of people referring to vital information such as age and sex as well as social and cultural factors.

Spirogram - An instrument that measures the amount and rate of air exchange in the lungs.

SR - Stirling/Raymond, unexposed control area, south of Lethbridge, which is the main comparison area with IA.

SR-M - Stirling/Raymond minus Mormons, a subgroup found to be the best match for comparison to DCCI.

Standardized Incidence Ratio (SIR) - The ratio of the observed number of incident cancers divided by the number of expected cancers where the latter is obtained by applying to

the Index Area 1970 cohort, age-, sex-, and cohort-specific incidence rates derived from referent populations. (See definition of SMR for the description of a similar ratio applying to deaths.)

Standardized Mortality Ratio (SMR) - A rate which expresses the number of observed deaths in a defined area for a defined period compared to those you would expect if the rates of a reference population (such as an entire province) applied in the area concerned. For instance, if there were 75 observed deaths in a particular area during a decade and one expected 100 deaths in that same area given the provincial rates, the SMR would be 0.75. In situations where there is neither an excess nor a deficit of deaths in a given area the SMR is very close to 1.0 (unity).

Statistical significance - A statement that indicates the likelihood that differences in numbers or rates or averages observed could have arisen by chance alone.

Supplemental Incidence Period - January 1, 1985 - December 31, 1985.

Symptoms - Perceptions which people have about themselves or about their body which are indicators of possible disease. Symptoms are reports of persons as patients as they describe what they feel and are generally considered to be subjective findings.

Toxicology - A science that deals both with poisons and other substances to link their effect with health problems.

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SOUTHWEST ALBERTA MEDICAL DIAGNOSTIC REVIEW PROJECT

1. INTRODUCTION

In response to a "Request for Proposal" (RFP) (Appendix 1) released by the Acid Deposition Research Program (ADRP) of the Province of Alberta, we conducted a project to obtain needed scientific information on health outcomes for citizens living in an area of Southwest Alberta exposed to emissions that are a consequence of the industrial treatment of sour gas for over 28 years. This area has been designated as the Index Area in the terminology used by this project and adopted in this Report. It includes the communities of Twin Butte, Hill Spring, Glenwood, Mountain View and Willow Creek (hereafter termed Index Area in this report) with surrounding areas as shown in the map (Figure 1/1).

Extensive background information has been published by the Acid Deposition Research Program (ADRP) which originated the request for this proposal. The following section includes excerpts from the Request for Proposal which describes the mandate and objectives of the ADRP.

1.1 Acid Deposition Research Program: An Introduction

The potential adverse impact of acid-forming emission is one of the most significant environmental problems to be encountered in North America in the last two decades. Apart from proven effects on the environment, considerable research is to be initiated regarding the potential effects that these emissions may have on the health of humans, either directly through absorption and inhalation of the emissions or indirectly through ingestion of food and water.

In Alberta, the development of sulphur-containing natural resources results in the release of acid-forming emissions (e.g. SO_x, NO_x, H_2S) and other associated compounds (e.g. metal particulates, organics). The concern that these emissions may affect the health of Alberta citizens in the Index Area has been the topic of considerable discussion over the last twenty years, particularly in relation to the development of the sour gas industry. Numerous studies and public hearings have been conducted and several reports with attendant recommendations exist to try to resolve this issue. Despite these efforts, it is still unclear whether a direct cause-effect relationship exists between exposure to these emissions and reported health complaints and what role, if any, numerous confounding variables such as lifestyle may play in this problem.

In response to the continuing concern and efforts of many individuals within Government, industry and the public sectors to resolve this question, the Alberta Government and a consortium of industries created jointly the Acid Deposition Research Program (ADRP) to:

- develop a comprehensive understanding of the effects of acid-forming emissions on the environment;
- provide a scientific basis for sound long-term environmental management and regulatory control of these emissions;
- disseminate such information among members, to the public and to government bodies;
- undertake any research deemed appropriate;

- encourage and include opportunities for public representation in the ADRP.*

The Request for Proposal also cites the consensus (reached at an ADRP-conducted workshop in 1983) of a 23-member international panel, representing 17 areas of medical and toxicological expertise, that a comprehensive medical diagnostic review is necessary in the Index Area to determine the nature and magnitude of long-standing health complaints which residents ascribe to emissions from sour gas plants. In answer to the RFP we proposed a controlled diagnostic review study to determine whether the residents of the Index Area (Figure 1/1) experience adverse health effects more frequently than expected. The results of such a study, rigorously carried out, will then determine what additional environmental or health related studies are indicated.

On May 1, 1985 it was announced to Albertans at a public meeting that a study designated 'Medical Diagnostic Review' would begin in the summer of 1985 with the McGill Interuniversity

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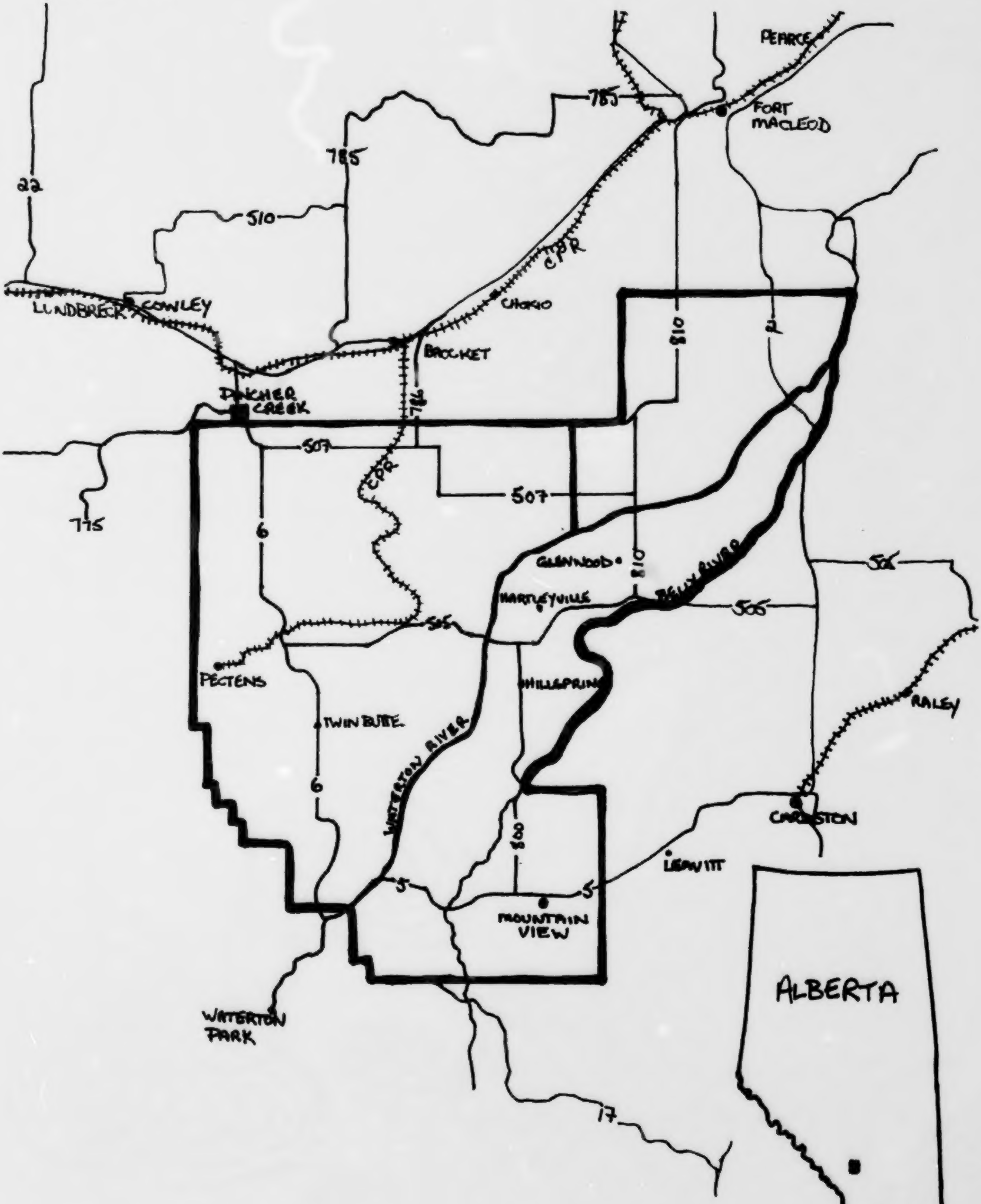
* Objective added to ADRP charter since RFP.

Research Group undertaking the work. The study would be funded by a grant from Alberta Community and Occupational Health (formerly Alberta Social Services and Community Health) and administered by the Acid Deposition Research Program.

Figure 1/1


PEARCE
785
FORT MACLEOD
785
22
510
CPR
CHOKIO
LUNDBRECK
COWLEY
BROCKET
PINCHER CREEK
786
507
CPR
507
775
6
GLENWOOD
810
810
2
BELLY RIVER
HARTLEYVILLE
505
505
505
PECTENS
HILLSPRING
TWIN BUTTE
WATERTON RIVER
RALEY
6
800
CARDSTON
LEAVITT
5
5
MOUNTAIN VIEW
WATERTON PARK
17
ALBERTA

1.2 Advisory Boards, Committees and Liaison Staff

1.2.1. Scientific Advisory Board

Chronologically, the Scientific Advisory Board (SAB) was the first to be assembled. The SAB authorized the Request For Proposal which gave the broad objectives guiding the initial protocol prepared and submitted by the investigators. They later reviewed the protocol submitted, proposed certain changes, most of which were readily accepted by the investigators, and gave scientific clearance to proceed with the basic design and objectives set forth in the application submitted by the McGill Interuniversity Research Group to the ADRP. The SAB made a site visit to the field site in July of 1985 and inspected arrangements there. They also approved certain modifications to the protocol requested by the investigators on the basis of what had been encountered in the field or to solve problems that had been unanticipated at the time when the initial proposal had been submitted. The main change made in July 1985 was authorization to increase the sample size of the unexposed control area (Stirling/Raymond - SR) so that sufficient number of non-Mormons would be selected with an aim to contrast with the representative exposed area (Didsbury, Carstairs, Crossfield, Irricana - DCCI). Lastly, the SAB reviewed and commented on the methods report as well as the results and conclusions of the investigators prior to formal transmittal of the Final Report to the Minister of Community Health and Social Services and to the Co-Chairmen of the ADRP. The names and affiliations of the members of the Scientific Advisory Board are given at the end of this chapter (Figure 1.2/1).

1.2.2 The McGill Scientific Advisory Group

In order to reduce any chance of inadvertent errors of analysis or interpretation, the Principal Investigator, with authority from the Dean of the Faculty of Medicine of McGill University, appointed a Scientific Advisory Group (SAG). The purpose of this group was to give the data an in-depth, exhaustive scrutiny. This was to insure that there were no avoidable errors of analysis, inference, or interpretation. This group is a panel of epidemiologists, environmental scientists, toxicologists, and clinical investigators, many with world-wide reputations, who helped to make sure that no stone was left unturned to enhance objectivity and accuracy of the Final Report. The list of the McGill Scientific Advisory Group and their affiliations is also attached at the end of this chapter (Figure 1.2/2).

1.2.3 Community Advisory Boards

A unique feature of this project was the formal creation of three Community Advisory Boards (CAB) to complement the work of the Scientific Advisory Board. The Scientific Advisory Board had judged primarily on the scientific merit of the work proposed. The Community Advisory Boards had a mandate to comment and approve the relevance of the proposed studies. Each of the three communities studied had such a Board and many meetings were held with them during planning, execution and follow-up of this study. Of major importance is the fact that the CAB (especially in the Index Area) assisted the team of investigators at each step of the way in major matters of practical implementation. They helped overcome barriers to community participation, enhanced community understanding of the aims of the project, and also helped solve many logistical problems that could have compromised the field work. They were invaluable in the process of identifying and confirming the identity of outmigrants. We attribute the high response rates attained in all areas in large measure to the Community Advisory Boards. We list the members of the Community Advisory Boards indicating their home communities at the end of this chapter (Figure 1.2/3).

1.2.4 Ethics Committee

Prior to implementation of the study in the field, an Ethics Committee was mandated by the Faculty of Medicine of McGill University to review all implications of ethical relevance, most particularly those potentially affecting the participants in the Index Area and the control areas. The Ethics Committee included experts in the scientific domains concerned, lay persons from the Montreal area, one prominent citizen of Southern Alberta who had the confidence of the population to be studied, and representatives of the Alberta Government and of the ADRP. The guidelines followed in reviewing the protocol from an ethics perspective were those of the Medical Research Council of Canada. The composition of the Committee, as well as the process complied with those published guidelines. The guidelines protect the anonymity of the reviewers and thus names are not listed here with respect to this Committee.

1.2.5 Professional Counsel and Coordination in Communications

In a project of high visibility and of enormous perceived importance by the public at large, it is important to reach a balance between the need of the public to be informed, and the need for professional media to have access to information in a manner that facilitates interpretation of what is happening, while protecting the confidentiality of participants and certain design aspects of the study that could have been hampered by excess publicity. For instance, it would have been inappropriate to publicize the relative importance of the target outcomes under assessment while the field work was in progress. If that had happened, there would have been a very high probability of biasing the results.

Coordination of communications was done by Ms. Jean Andryiszyn of the Calgary firm of Francis, Williams and Johnson who also served as Coordinator of Communications for the ADRP. The assistance and professional advice given resulted in a very satisfactory relationship of mutual support between the investigators and the media and a constant flow of information to the public. The smooth functioning of the communications aspects of the project is another important factor in attaining high response rates in all areas.

1.2.6 Support Staff of the Acid Deposition Research Program

In the phase of formulation of the Request For Application Dr. Robert Rogers served as Coordinator and shepherded the application and approval process through to the time when the field work began in Alberta in early June, 1985. From early June through the conclusion of the project Dr. Robert Wallace functioned as Program Manager and contact person of the funding agency. From his base in Calgary he made enormous contributions on a weekly and sometimes daily basis in the phase of field work to help assure that all the operational objectives were attained. There was no interference in the scientific conduct of the study from the ADRP staff, the administrative and physical intermediaries or the Government of Alberta which indirectly and ultimately funded most of the budget of the study.

Figure 1.2/1

SCIENTIFIC ADVISORY BOARD MEMBERS

Dr. Benjamin Burrows
Professor of Internal Medicine
Director
Division of Respiratory Sciences
College of Medicine
University of Arizona

Dr. Zoltan Annau
Professor
Department of Environmental Health Sciences
The Johns Hopkins University
School of Hygiene and Public Health

Dr. Jonathan M. Samet
Associate Professor of Medicine
Department of Medicine
University of New Mexico

Dr. Gerry B. Hill
Director
Department of Epidemiology
Alberta Cancer Board
Edmonton, Alberta

Dr. Walter Mertz
Director
Human Nutrition Research Centre
Agriculture Research Centre
U.S. Department of Agriculture

Dr. Mark J. Utell
Associate Professor of Medicine and Toxicology
University of Rochester School of Medicine

Figure 1.2/2

SCIENTIFIC ADVISORY GROUP MEMBERS

Dr. Dwight Janerich
Professor and Head
Cancer Program
Department of Epidemiology
and Public Health
Yale University
School of Medicine

Dr. David Schottenfeld
Chief Division of Epidemiology
Memorial Sloan Kettering
Cancer Center
Chairman Designate
Department of Epidemiology
University of Michigan

Dr. John Bailar
Department of Biostatistics
Harvard School of Public Health
Statistical Consultant
New England Journal of Medicine
Senior Executive Advisor
Office of Disease Prevention
and Health Promotion, U.S. DHHS

Mr. Allan Penn
Senior Environmental Science Advisor
Cree Nations Council of Quebec

Dr. Jean-Yves Savoie
Chemist and Scientific Director
Institut de Recherche en
Sante et Securite au Travail
Province of Quebec

Dr. Patricia A. Buffler
Professor of Epidemiology
Epidemiology Research Unit
The University of Texas
Health Sciences Centre at Houston

Professor Roy Acheson
Head, Department of Community
Medicine
Cambridge University
School of Clinical Medicine
Addebrooks Hospital

Dr. Michel Ibrahim
Dean and Professor of
Epidemiology
School of Public Health
University of North Carolina
Chapel Hill, North Carolina

Dr. Sonia Buist
Professor of Medicine
Professor of Physiology
Department of Physiology
University of Oregon Medical
School

Figure 1.2/3

COMMUNITY ADVISORY BOARD

INDEX AREA	REPRESENTING
Mrs. Sophie Taylor Pincher Creek	(Twin Butte)
Mr. Tom Ferguson Pincher Creek	(Twin Butte)
Mr. Jack Ady Hill Spring	(Hill Spring)
Mrs. Margaret Caldwell Hill Spring	(Hill Spring)
Mr. Noel Pilling Mountain View	(Mountain View)
Mrs. Laura West Mountain View	(Mountain View)
Mr. Wayne Smith Glenwood	(Glenwood)
Mr. Rudy Kutsch Glenwood	(Glenwood)
Mrs. Ellen Chester Fort Macleod	(Willow Creek)
Mr. Arthur Mathes Pincher Creek	(Industry Rep.)

Figure 1.2/3 Community Advisory Board -- continued

DIDSBURY, CARSTAIRS, CROSSFIELD, IRRICANA (DCCI)

Jessie Alcorn
Councilor
Carstairs

David Derksen
Deputy Reeve
Carstairs

Louise Feltham, M.D.
Councilor
Rocky View

Lorne Kosack
Deputy Mayor
Crossfield

David Lord
Mayor
Irricana

Brian Popp
Hospital Administrator
Didsbury

Wayne M. Ryder
Town Manager
Crossfield

Ron Stoutenberg
Administrator
Irricana

Don Watt
Mayor
Didsbury

STIRLING/RAYMOND

Marvin Dahl
Councilor
County of Warner

Dennis Fromm
Councilor
Raymond

John Maloney
Stirling Senior Citzens

Ken Moore
Mayor
Stirling

Terry Bland
Chairman
Positive Response Committee
Stirling

Don Nilsson
Councilor, Stirling

Dick Papworth
Reeve County of
Lethbridge

Arlene Sillito
Stirling Village
Office

Brad Watson
Town Office
Raymond

2. PURPOSE

The original protocol set forth the following objectives. After field work was underway and feasibility checks had been completed some modifications were made with approval of the SAB.

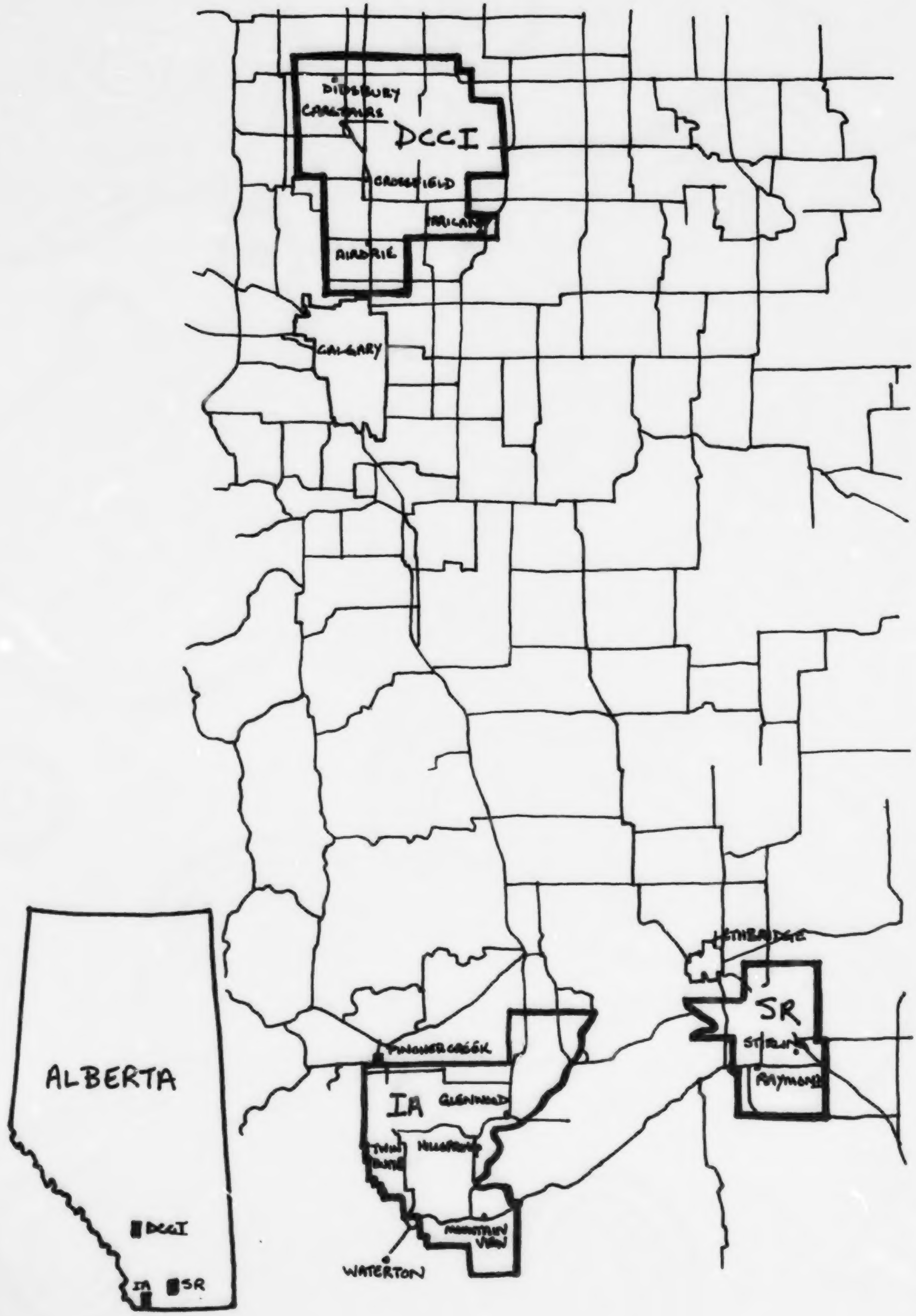
2.1 General Objectives at the Outset

The purpose of this study was to determine whether the residents of the Index Area (IA) experience adverse health effects more often than is expected from frequencies derived or observed:

1) In two carefully selected control areas within Alberta, one that is demographically similar to the Index Area in all respects, but not exposed to sour gas refineries and one that is representative of southern non-metropolitan Albertans exposed to sour gas.
2) In the general population of Alberta.
3) In subsets of the entire Canadian population where either similarities or contrasts could be illuminating.

Figure 2.1/1 shows the Index Area and the control areas within Alberta which were eventually selected as reference populations. See Chapter 4 for the methods employed to select the reference areas.

Figure 2.1/1


DIDSBURY
CARSTAIRS
DCCI
CROSSFIELD
IRRICANA
AIRDRIE
CALGARY
LETHBRIDGE
SR
STIRLING
RAYMOND
PINCHER CREEK
IA
GLENWOOD
TWIN BUTTE
HILLSPRING
MOUNTAIN VIEW
WATERTON
ALBERTA
DCCI
IA
SR

2.2 Specific Research Objectives Set Forth in the Protocol

These are the specific research objectives of the study:

1) Determine the frequency of health problems and diagnoses among residents of the IA that are alleged to be associated with the type of industrial pollution found in the vicinity.

2) Determine, for comparison, when feasible, the frequency of similar health problems in (i) Alberta as a whole, (ii) all rural areas of Alberta that are geographically and demographically similar, (iii) other rural areas in Canada that are demographically similar, and (iv) other areas from anywhere in Canada where data gathering tactics similar to those employed by the Canada Health Survey had been used. The reference areas that proved to be feasible are the population in Toronto from the Junction Triangle study, Southern Alberta, and Canada using Canada Health Survey data (see definitions, Figure 9.1/1).

3) Determine, empirically, the current frequency of health problems and diagnoses of the type alleged to be associated with exposure to the emissions of the sour gas industry in the Index Area and two comparable areas of Alberta. One of these "control" areas is sociodemographically very similar to the Index Area and not exposed to the sour gas industry.

The other is also sociodemographically representative of Southern rural Albertans as a whole, but is exposed to sour gas emissions.

4) Determine whether the current frequencies of these health problems and diagnoses for the IA differ in any way from those in the two areas selected as controls.

5) Determine whether the incidence of and mortality from cancer - both for all cancers and for selected cancer categories in the IA differ, in any way, from those in census tracts elsewhere in Alberta chosen for their sociodemographic similarity and whether they differ in any way from the cancer incidence experience of Alberta as a whole.

6) Determine whether the frequency of ascertainable reproductive abnormalities and birth defects differ from that observed in demographically similar areas elsewhere in Alberta, in the Province as a whole and in any well-defined Canadian jurisdiction for which good quality numerator and denominator data can be obtained. The contrasts with reference populations had to be limited to the control groups in the study in view of constraints detailed in Chapter 7.

7) Determine the frequency of disability and debility days

experienced by the study population in the IA and the control areas, and then compare it with rates derived in the Canada Health Survey for the Prairies and Canada.

8) Evaluate the severity of adverse health outcomes, if any, observed in the IA, and describe their clinical, social, and economic significance mainly through comparison with the control areas.

9) Determine, through clinical and laboratory strategies the extent of any evidence of contamination of IA residents with selected heavy metals and other substances alleged or shown to be noxious to health.

10) Determine average annual mortality in the IA and compare it to the rates in the control areas and primarily with that of Alberta as a whole.

11) Determine whether there is any temporal, geographic, or clinical clustering of any adverse health phenomenon that might provide insight into the possible effects of relevant exposures.

12) Report all of the findings in a manner that is both uncompromising with regard to their scientific and analytic admissibility, as judged by peer reviewers, and

understandable to the general public, governmental policy makers and health providers who will use the data as the basis for public health policy affecting citizens similarly exposed.

3. ADMINISTRATION OF THE MDR PROJECT AND LOGISTIC ACCOMPLISHMENTS

3.1 Introduction

On May 2, 1985 in Pincher Creek the Government of Alberta and members of the ADRP officially announced that the Rapid-Response Unit of the Division of Clinical Epidemiology of the Montreal General Hospital had been given the mandate to conduct the Southwest Alberta Medical Diagnostic Review (MDR) Project.

In the weeks preceding this official announcement, the research team's Administrator, Ms. Anne Roussell, met with two members of the ADRP administration, Drs. Robert E. Rogers and Dennis Stokes to review the different options available in Alberta regarding staff lodging, clinical facilities, and possible suppliers. However, most of the leased medical supplies were obtained from Montreal to insure that we had everything that was required on site to begin seeing participants on June 1.

Since it was impossible to have the Administrator in Alberta immediately after formal approval of the research project; it was decided to appoint a Site and Transportation Manager who could leave for Alberta immediately. Mr. Arthur Allan was appointed to that position. On May 2nd, Mr. Allan was present at the public announcement of the grant award at Pincher Creek and remained in Alberta to begin preparations for the field work. Mr. Allan and Ms. Roussell worked together from that time on to insure that all logistical aspects of the study were handled efficiently.

3.2 Personnel

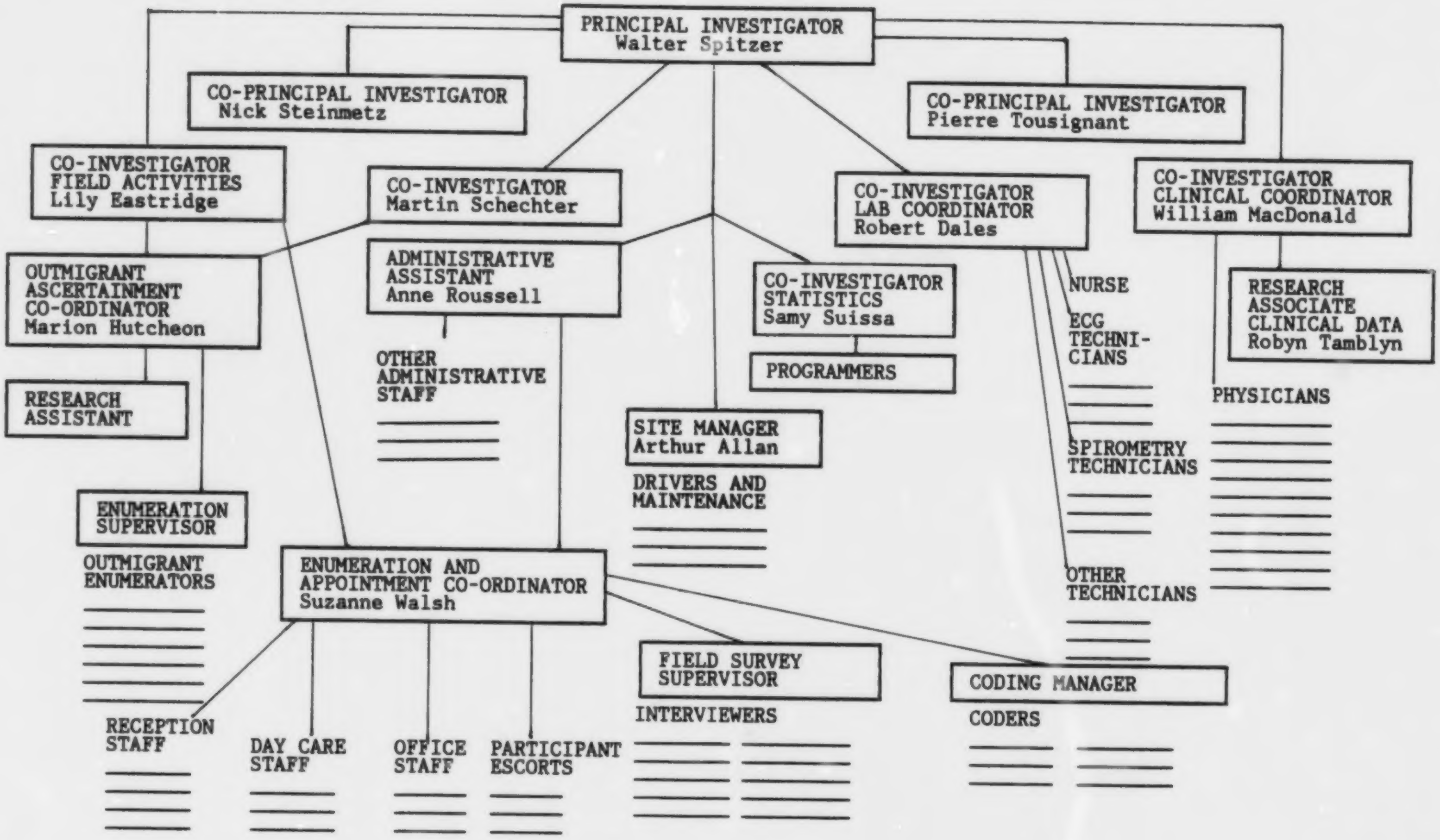
In order to be fully prepared to start the field work on June 1, 1985, it was necessary to train part of our staff in Montreal. The most important concerns were the training of physicians, interviewing staff, and laboratory technicians.

The first step was the recruiting and training of interviewers. They were made familiar with the administration of the questionnaires, and with issues of validity and reliability in the field.

Training of the laboratory staff was done through representatives of the following institutions: McGill University Department of Epidemiology and Biostatistics Respiratory Function Laboratory, Royal Victoria Hospital and the Montreal Chest Hospital's Departments of Electrocardiography, Foothills Hospital's Department of Clinical Chemistry, and the Centre de Toxicologie du Québec.

As far as the other staff were concerned, most of the recruiting was done in Montreal but no training was done prior to the research team's arrival in Alberta. Figure 3.2/1 summarizes the relationship and general lines of accountability of scientific, professional, administrative, and support staff throughout the summer.

Figure 3.2/1


PRINCIPAL INVESTIGATOR
Walter Spitzer
CO-PRINCIPAL INVESTIGATOR
Nick Steinmetz
CO-PRINCIPAL INVESTIGATOR
Pierre Tousignant
CO-INVESTIGATOR
FIELD ACTIVITIES
Lily Eastridge
CO-INVESTIGATOR
Martin Schechter
CO-INVESTIGATOR
LAB COORDINATOR
Robert Dales
CO-INVESTIGATOR
CLINICAL COORDINATOR
William MacDonald
OUTMIGRANT
ASCERTAINMENT
CO-ORDINATOR
Marion Hutcheon
ADMINISTRATIVE
ASSISTANT
Anne Roussell
CO-INVESTIGATOR
STATISTICS
Samy Suissa
NURSE
ECG
TECHNI-
CIANS
RESEARCH
ASSOCIATE
CLINICAL DATA
Robyn Tamblyn
PROGRAMMERS
RESEARCH
ASSISTANT
OTHER
ADMINISTRATIVE
STAFF
SITE MANAGER
Arthur Allan
PHYSICIANS
SPIROMETRY
TECHNICIANS
DRIVERS AND
MAINTENANCE
ENUMERATION
SUPERVISOR
OUTMIGRANT
ENUMERATORS
ENUMERATION AND
APPOINTMENT CO-ORDINATOR
Suzanne Walsh
OTHER
TECHNICIANS
FIELD SURVEY
SUPERVISOR
CODING MANAGER
INTERVIEWERS
CODERS
RECEPTION
STAFF
DAY CARE
STAFF
OFFICE
STAFF
PARTICIPANT
ESCORTS

3.3 Transportation

From Montreal: In order to take advantage of low-cost airline fares, it was necessary to proceed immediately. With the assistance of our travel agent in Montreal, we were able to benefit from a large number of "super-saver" tickets and, therefore, receive a few free seats from Air Canada. We scheduled three departures from Montreal, one on May 28, another in mid-June and the final one on June 28. In addition to this, we had to provide transportation for those people arriving from Winnipeg and Vancouver. In total, we arranged for 123 departures for Southern Alberta during the period May 1 to August 31, 1985.

Within Alberta: For the duration of our stay in Alberta, we leased six 12-passenger vans and eight cars. Initially, these were to be used to transport participants to/from the sites. However, following a meeting with the Community Advisory Board members, the general consensus was that participants preferred to use their own vehicles. Therefore, the vehicles were used to transport staff to/from the working sites, to participants' homes when necessary, to move equipment, and to move laboratory specimens.

In addition to the above vehicles, we had the use of a small leased single-engine aircraft. This allowed us to transport frozen and chilled blood samples to Calgary more rapidly. It also permitted senior staff to travel the long distances from one site to another in a much shorter time than car transport would have. At peak periods during late July through mid-August we leased a second single-engine aircraft for rapid transportation of cooled or frozen blood samples, equipment, and data.

3.4 Staff Lodging

3.4.1 Index Area

On May 3, 1985, Ms. Roussell and Mr. Allan met with the owner of the Kilmorey Lodge. The Kilmorey Lodge was considered to be the best facility for the group, which at that time was estimated to be approximately 75 people. It was conveniently located in Waterton Lakes National Park, which was within reasonable driving distance to Hill Spring. However, during the course of the summer, our staff increased by approximately 40 to 50 people and it was necessary to rent additional rooms in other motels located in Waterton. Once the group was divided in early August to move to the control areas, these additional facilities were no longer necessary.

3.4.2 Control I - Stirling/Raymond (SR) Area

On July 23rd, a staff of approximately 30-40 people were transferred to this area. Since these are rather small communities, it was necessary to find housing facilities in Lethbridge. Mr. Arthur Allan moved to the area a few days in advance to investigate what hotels/motels were available for such a large group. It was decided to move our staff to the Lethbridge Lodge because of its facilities and proximity to the working site.

3.4.3 Control II - Didsbury-Carstairs-Crossfield-Irricana (DCCI) Area

In early August, approximately 60 people were transported to control area II. The group included the administration staff as well as coders and computer personnel. Following recommendations from the ADRP, our staff was lodged at the Marlborough Inn in Calgary. The Marlborough Inn provided us with the use of four offices, one for administration, one for coding, one for the Principal Investigator, and a fourth one which was used for filing and telephoning participants to set appointments. The hotel was located near Highway 2, approximately 25 km from our work site at the Crossfield Curling Club grounds.

3.5 Meals

At the Kilmorey Lodge in Waterton, meals were prearranged in the contract with the Lodge. In May and early June we were given menu choices. However, once the group increased, a buffet-type selection was initiated. Box lunches were brought from the lodge to Hill Spring, where we stored food in a kitchen-diner trailer.

Once the group was separated and relocated in the control areas, a system of meal tickets was initiated. Arrangements were made with either the hotel or a local caterer for boxed lunches at the working sites. Contrary to the Kilmorey Lodge in Waterton, the Marlborough Inn and the Lethbridge Lodge provided meal selections from their usual menus.

3.6 Clinical Facilities

3.6.1 Index Area

In early May, Mr. Arthur Allan negotiated with several mobile trailer companies. It was decided that Atco Trailers in Calgary could provide the units we required with the rigid deadlines we set. Between the period of May 28 and June 1, eleven trailers were set-up in Hill Spring as displayed in Figure 3.6/1.

Another important aspect of setting up these facilities was to insure that we had electricity, sewage, and telephone lines. Mr. Allan made the necessary contacts with TransAlta Utilities to insure that we could operate on June 1 as scheduled. Installation and proper operation of such utilities usually takes approximately four to six weeks. Mr. Allan was able to have all services functioning properly by June 1.

3.6.2 Control Areas

In late July when the group was moved to the control communities, only four trailers remained in Hill Spring. Six trailers were moved to Crossfield and the other was returned to Atco. In Crossfield, we had the use of the Crossfield Curling

Figure 3.6/1

Club building and the trailers were parked on the club's grounds. In the second control area, we were fortunate to have access to the Stirling school facilities. This allowed us to expand our facilities and eliminate the cost of additional trailers. The four trailers left in Hill Spring were used for the Outmigrant Study survey and as a small laboratory facility to do repeat spirometry determinations.

3.7 Medical Equipment/Supplies

As mentioned earlier, the deadlines we faced were quite an obstacle to overcome. It was necessary to contact several large medical suppliers before we were able to find one that could provide us with the proper equipment. Since the equipment required was very sophisticated and costly, suppliers were hesitant to lease rather than sell the equipment. By explaining the purpose of our study, we were able to convince them that we were not in a position to buy equipment for eight weeks.

The following is a list of suppliers from above whom we leased and/or purchased medical equipment/supplies:

- Ingram and Bell Medical (Calgary)
  Rental of ECG machines and purchase of supplies

- Bionetics (Montreal)
  Rental of spirometry equipment/supplies

- Medi-Plus (Montreal)
  Rental of all small medical equipment and purchase of supplies

- Westcare Medical (Lethbridge)
  Purchase of medical supplies

- Fisher Scientific (Edmonton)
  Purchase of laboratory equipment

- CANLAB (Edmonton)
  Purchase of laboratory equipment

3.8 Winter Reassessment Logistics

In order to determine possible seasonal variations in symptoms and short term disability a Winter Reassessment, to be described later, was carried out in the IA and SR areas.

3.8.1 Personnel

The Winter Reassessment was carried out by a team of 11 people. From this group, an advance team of four were sent from Montreal to the IA and SR on January 14, 1986 a week prior to data collection. Their task was to make appointments for laboratory recalls from the sample list provided, update the address list on outmigrants, and set-up the testing facilities.

The remaining staff of seven arrived on January 20, and were divided between Glenwood in the IA Area and Stirling in the SR area, with each site supervised by one co-principal investigator. One back-up physician and one interviewer were available to fill in as necessary. Arrangements had been made for a team of four people to remain as long as was necessary, in the event weather conditions delayed the study.

Halfway through the study period, the two investigative field teams switched sites to control for any bias inherent to the investigators.

3.8.2 Travel Arrangements

Three small vans and one station wagon were leased for the entire duration of the Winter Reassessment.

3.8.3 Accommodations

The Heritage Inn in Pincher Creek and the Lethbridge Lodge in Lethbridge were selected as living quarters. These hotels were approximately 30 km from the work sites.

3.8.4 Working Sites

Physical arrangements: Following recommendations from the Community Advisory Boards in both areas, we selected the Glenwood Church for conducting work in the Index Area and the Senior Citizen Centre in Stirling for the control area. To assist us we had the collaboration of a Community Advisory Board member resident of each of the two areas; Mrs. Salmon in Stirling and Mr. Kutsch in Glenwood.

Each site was set up as follows:

- 1 large room was used for reception and waiting area;
- 1 room for the ritualistic medical examination;
- 1 room for interviewing;
- 1 room for spirometry.

Two temporary telephone lines were installed by AGT Telephones in each site for the period Monday, January 20 to Friday, January 30. Initial telephone calls for setting up appointments were made from the hotels, where the advance team were stationed, following recommendations from AGT in Lethbridge to help reduce costs.

3.8.5 Equipment

Each physician provided his own medical equipment for the ritualistic medical examination. Two spirometers were rented from Bionetics in Montreal as had been the case in the summer. All other supplies were transported from Montreal to insure that all would be in readiness for this short exercise.

The Winter Reassessment was completed without difficulty. The weather was ideal for transportation as well as participation. All equipment and supplies arrived on time, telephone installations were completed as scheduled, and the working sites proved to be ideal.

3.9 Summary of Chronology of Major Events of the Project

3.9.1 Planning

December 1984	"Request for Proposal" released by the ADRP.
February 10, 1985	Submission for proposal sent to the ADRP, senior members hired.
March 1985	Meeting in Atlanta with the Scientific Advisory Board, the main investigators, and the ADRP.
April 1985	Agreement in principle reached in Edmonton. Recruiting of physicians begins, trip to Alberta to arrange for trailer rentals and accommodations. Site Manager arrived to make contacts and set up the site.
May 1, 1985	Official announcement of the project made in Pincher Creek, Alberta by the Minister and Deputy Minister of Health and the Program Manager from the ADRP.

May 3, 1985	First meeting with the Community Advisory Board.
May 1985	Development of questionnaires and data-gathering instruments.
	Final accommodation arrangements made.
	Hiring of support staff, interviewers, and coders.
	Training of interviewers and coders.

3.9.2 Field Activities

May 28, 1985	Five senior personnel arrive in Alberta.
May 31, 1985	Thirty staff members arrive in Alberta.
June 1985	Enumeration of Index Area.
June 1-2, 1985	Initial training of ritualistic physicians.

June 4-5, 1985	Set up of clinical supplies, coding area, and computers.
June 6, 1985	Saw first participant.
June 28, 1985	Arrival of the remaining staff.
July 4, 1985	Seeing approximately 60 participants per day.
July 8, 1985	Seeing 70-80 participants per day.
July 1985	Arrangements made for sites in two control areas.
July 1985	SAB visit and revision of protocol.
July 24, 1985	First participants seen in the Stirling control area.
July 28, 1985	On-site inspection of clinical facilities and laboratories by the SAB.

August 3, 1985	Successful completion of field work in the Index Area.
August 5, 1985	Beginning of outmigrant enumeration.
August 8, 1985	First participants seen in the Crossfield control area.
August 24, 1985	Successful completion of field work in both control areas.
September 6, 1985	Completion of data entry and community verification of the outmigrant list for all three areas.

3.9.3 Data Verification, Analysis and Production of the Final Report

October 1985	Opening of office in Calgary to process outmigrant returns and contact outmigrants to encourage their response.
October 15, 1985	Outmigrant questionnaire mailout begins.

October 21, 1985	First analysis retreat--the Principal, Co-Principal, and Co-Investigators as well as various consultant personnel oversee the work to achieve the analytic goals set.
October 27, 1985	McGill University--Department of Epidemiology and Biostatistics seminar on the Alberta Medical Diagnostic Review.
November 1985	List of outmigrant names with missing addresses sent to the Bishop of the Latter Day Saints Churches in the Index Area.
November 11, 1985	Analysis retreat.
December 10, 1985	Analysis retreat.
Dec. 30-31, 1985	Second mailing to all outmigrants who had not yet responded to the questionnaire.
January 7, 1986	Analysis retreat.
January 14, 1986	Arrival in Alberta of the advance team for the Winter Reassessment Exercise.

January 15-30, 1986	Final attempts made to contact outmigrant sources for further information on outmigrants with missing or incomplete addresses.
January 22-30, 1986	Winter Reassessment Exercise.
February 1, 1986	Ad published in Lethbridge Herald listing remaining 106 outmigrants for whom we as yet had no address.
February 11, 1986	Analysis retreat.
March 6, 1986	Analysis retreat.
March 8-9, 1986	Intensive weekend writing session for the methods chapter of the final report.
March 21, 1986	Meetings with the genetics consultant for the reproductive study to review the work done and finalize the plan for analysis for this component.
March 25, 1986	Analysis retreat.

March 31, 1986	Deadline for mailing of outmigrant questionnaires to new names reported by outmigrant respondents.
April 5-6, 1986	Intensive weekend writing and editing session for finalizing the methods and methodological results of the final report.
April 14, 1986	Release of the introductory, methods, and methodological results chapters to the McGill Scientific Advisory Group.
May 8-10, 1986	Meeting of the McGill Scientific Advisory Group (SAG) in Montreal.
May 10, 1986	The Chairman of the McGill Scientific Advisory Group (Dr. Dwight Janerich from Yale University) leaves a memorandum of conclusions, criticisms, and recommendations with the Principal Investigator prior to his return to New Haven.
	The ADRP Scientific Advisory Board is sent (by courier) the same introductory and methods chapters of the report which the

McGill Scientific Advisory Group had received on April 14.

May 12-22, 1986	The McGill research team makes any revisions and changes deemed appropriate after receiving the criticisms from the McGill SAG.
May 23, 1986	The McGill research team sends the final draft of the result chapters of the report to the ADRP Scientific Advisory Board members (SAB) by courier.

3.9.4 The Final Report: Presentation and Follow-Up

May 30-June 2, 1986	The McGill Interuniversity Research Group meets the ADRP Scientific Advisory Board in Chicago for presentation, discussion and exchanges subsequent to peer review by the ADRP Scientific Advisory Board. The McGill group is ready to present the key findings orally in a manner similar to the presentation which will occur later in the Twin Butte/Pincher Creek area.

June 2-6, 1986	The McGill Interuniversity Research Group makes any changes that are deemed appropriate following SAB recommendations (the changes will be restricted to matters of substance on analysis and interpretation, rather than on style, which can be assumed will be in order).
June 6, 1986	A near-final draft of the report is delivered personally to the Minister of Social Services and Community Health.
June 10, 1986	The Principal Investigator presents the final report to the Co-Chairmen of the ADRP and the Minister of Social Services and Community Health.
June 11, 1986	The public meeting in Pincher Creek is held to release the report publicly to the Community Advisory Boards, the scientific peers in Alberta, the general public, and the media.
June 12-15, 1986	The Co-Principal Investigators interact with small groups of the communities in the Index Area to answer questions and interpret results.

June 19, 1986	Under the auspices of the Summer Advanced Studies Programme of the Faculty of Medicine of McGill University, an invitational scientific meeting is held to present the findings to the scientific community in Eastern Canada, Northeastern U.S.A. and selected scientists from other parts of the North America.

3.10 Comment

Since this was probably one of the largest clinical epidemiology field studies ever conducted in Canada, there was no model or precedent we could follow. Therefore, it was necessary to plan each step carefully and to insure that the proper resources were available. Our greatest asset was our highly committed team of advisors, investigators, and research staff that agreed to undertake this project on such short notice. The enthusiasm and determination of each and every one was a determining factor in the overall success of the field work. Each person carried out his or her assignment and as the summer progressed, everything fell into place like pieces in a puzzle. The ADRP Program Manager and the Communications Coordinator, both Albertans with intimate knowledge of the local scene, helped solve innumerable small and big problems. On August 24, 1985, the result of the collaborative effort was the successful completion of all summer field work in Alberta, one week earlier than originally anticipated with all response rate goals attained.

4. DESIGN OF STUDY

4.1 General Plan

The plan was to determine the health status of residents in the Index Area (IA) in the summer of 1985 and to compare the findings with those obtained from residents in the unexposed Stirling/Raymond (SR Area) during the same season, namely summer 1985. Another important comparison was made with residents typical of southern rural (non-metropolitan) Albertans living in rural communities north of Calgary surrounding and including Didsbury, Carstairs, Crossfield and Irricana (DCCI Area) who were also exposed to sour gas plant emissions. As indicated in the original research proposal the principal contrast we declared in advance is between the IA Area and the SR Area for health status as of 1985 evaluations. These are referred to as crossectional comparisons and are included in what we call the crossectional study. The crossectional survey was the most important and the most costly part of the project and is described in more detail in later chapters.

However, in Figure 4.1/1 we show that we have also conducted what in technical, scientific terms, is called a cohort analytic or a cohort comparison study. A cohort is an assembly of persons sharing common characteristics at a given point in time. In this project, there are two important dates that affect the strategy of following people over time. One is 1957, just before the first exposure to emissions from sour gas plants occurred in the Index Area. The most important reference point is 1970, for two reasons: i) Sufficient time had passed since 1957 so that delayed adverse health effects had had a reasonable chance to have become manifest by 1970. ii) The span of time between 1970 and 1985 provides sufficient years of follow-up to identify adverse health events of importance such as new cancers occurring since 1970, or of detectable diseases of the respiratory or neurological systems.

Thus, for purposes of a cohort strategy to study health problems in southwestern Alberta, the most important denominator of people delineated is the cohort of residents who lived in the Index Area. We made every effort to follow this cohort forward in time through August of 1985. We studied samples of the 1970 cohort of both the main control SR area, the DCCI, area as well as the IA.

Figures 4.1/1 and 4.1/2, show the relationship between cohort follow-ups and crossectional comparisons. In 1985, the people who lived in the Index Area included those who lived there in 1970 and had remained in the area for the 15-year interval.

Figure 4.1/1

RELATIONSHIP OF COHORT FOLLOW-UP AND CROSSECTIONAL COMPARISONS

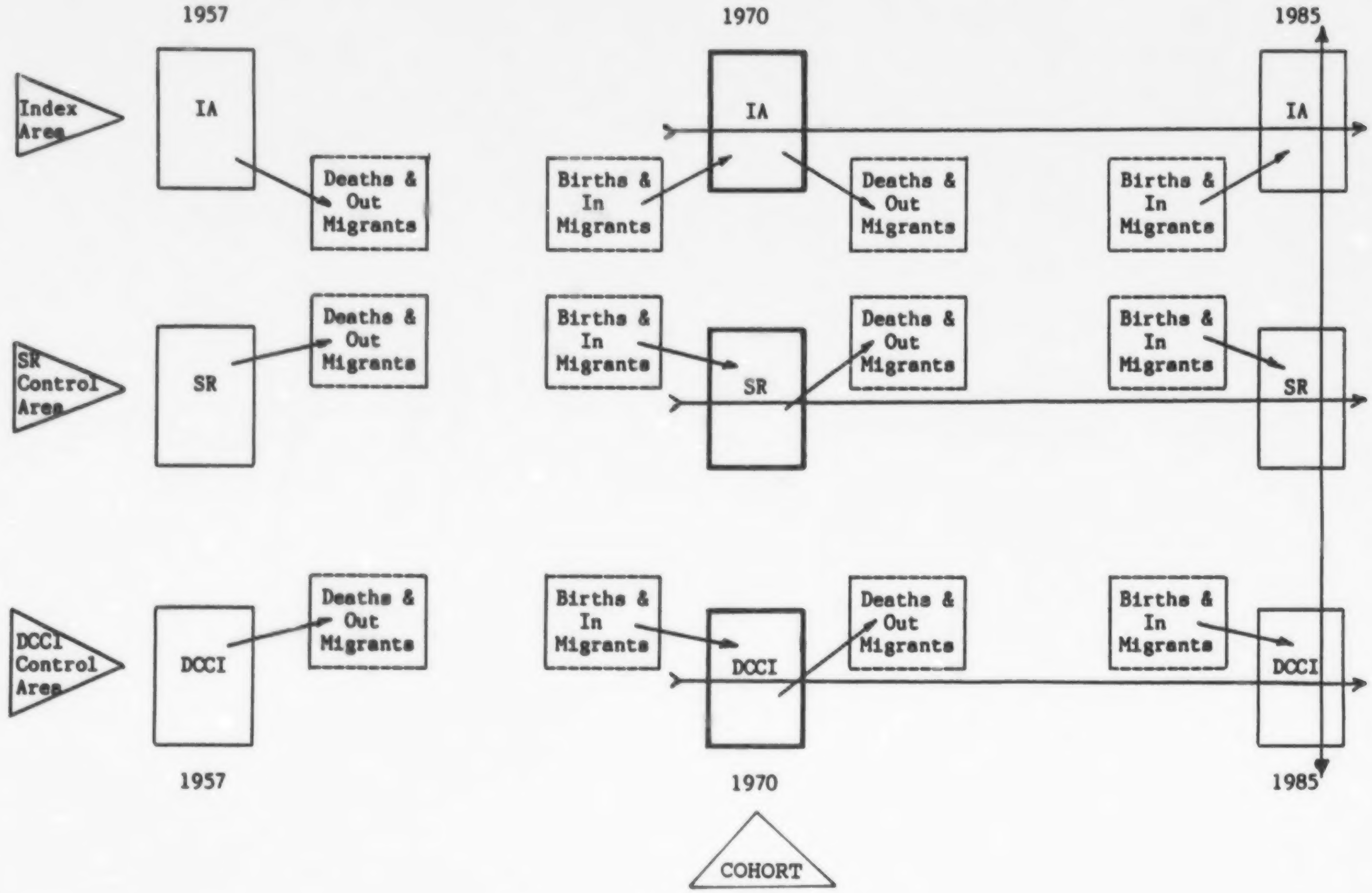
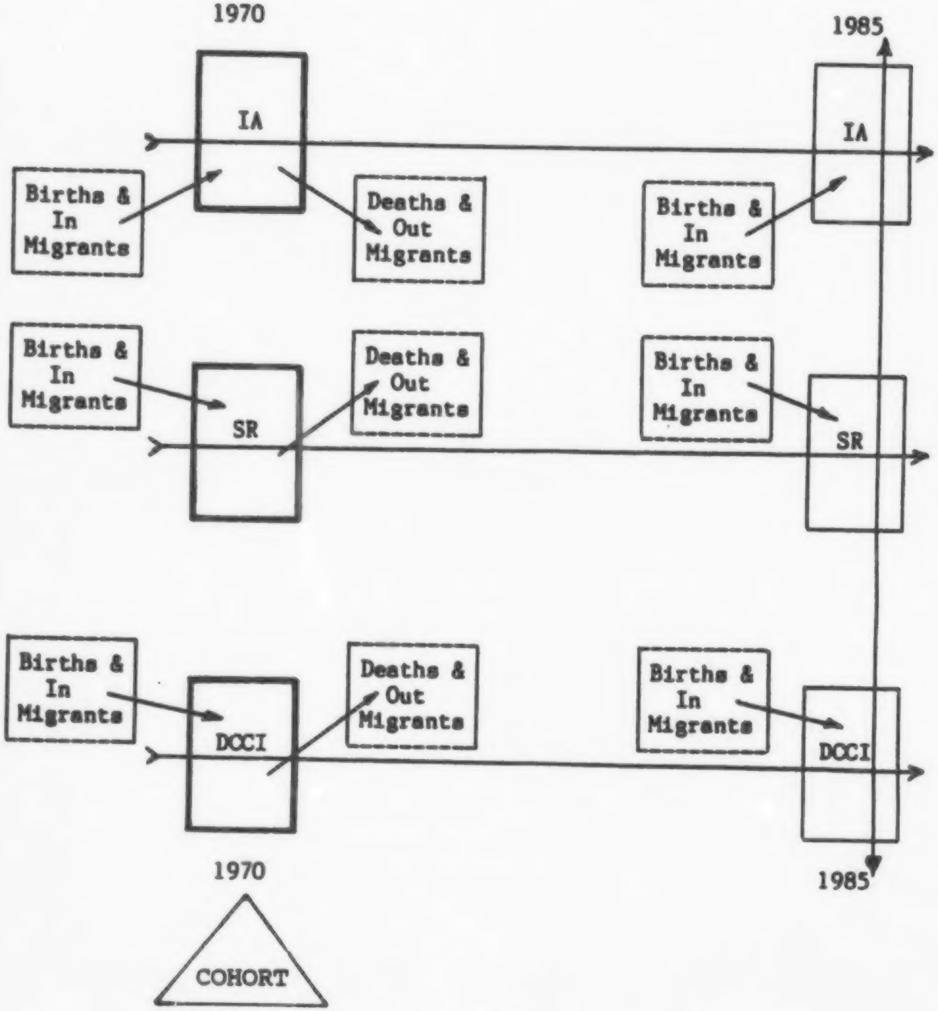

1957
1970
1985
Index Area
IA
Deaths & Out Migrants
Births & In Migrants
IA
Deaths & Out Migrants
Births & In Migrants
IA
SR Control Area
SR
Deaths & Out Migrants
Births & In Migrants
SR
Deaths & Out Migrants
Births & In Migrants
SR
DCCI Control Area
DCCI
Deaths & Out Migrants
Births & In Migrants
DCCI
Deaths & Out Migrants
Births & In Migrants
DCCI
1957
1970
1985
COHORT

Figure 4.1/2

RELATIONSHIP OF COHORT FOLLOW-UP AND CROSSECTIONAL COMPARISONS

(DETAILED)


1970
1985
IA
Births & In Migrants
Deaths & Out Migrants
Births & In Migrants
IA
Births & In Migrants
Deaths & Out Migrants
Births & In Migrants
SR
SR
Births & In Migrants
Deaths & Out Migrants
Births & In Migrants
DCCI
DCCI
1970
1985
COHORT

It also included children who had been born and remained in the area during that period of time as well as people who migrated in (inmigrants). However, if one is interested in the outcome or "fate" of the cohort of 1970 and wishes to reach some conclusions about the experience of that cohort contrasted to comparison cohorts, then one must take into account the people who lived in the Index Area in 1970 and who died as well as those who migrated out, (outmigrants).

The crossectional survey assesses those who lived in the Index Area in 1985 and compares them with those who lived in the SR and DCCI areas at the same time. For certain key target health outcomes or dependent variables such a crossectional comparison is adequate. This could apply to short-term and reversible phenomena such as selected symptoms. Therefore, to reach conclusions about some of the selected key variables identified in advance by the investigators, a crossectional examination sufficed. For certain adverse health outcomes that take years to develop, one must examine the experience of a cohort (in this case the 1970 cohort) which has had sufficient exposure (in this case since 1957) to be capable of exhibiting such adverse health outcomes. That cohort could also be followed forward from 1970 to 1985 to further establish whether such adverse outcomes were detectable and had in fact been occurring.

Another cohort not shown in Figure 4.1/1 will have been delineated through published information available through Statistics Canada. That is the experience of all of Alberta, and selected areas of southern Alberta alone. These cohorts were identified exclusively for the cancer component of this project and the methods are explained in the corresponding chapter.

The most important purpose of conducting a longitudinal follow-up of persons who were in the Index and Control Areas as of 1970 is to determine whether there had been selective unequal health-related migration in the Index Area compared to the main comparison area (SR Area). If those who were sicker than representative people now living in the Index Area had had a greater tendency to move out (or indeed to die) than those that remained behind, the findings in the crossectional comparison for long-lasting irreversible events would understate the degree of illness of all people who ever lived in the Index Area. If, on the other hand, only those who were well and energetic had had a tendency to move out leaving those who are sicker behind, the survey of the people left in the Index Area would also give a false or spurious impression; remaining Index Area residents could then be expected to be sicker than those in the principal comparison area.

In the balance of this chapter, we give a general overview of the plan of the Southwest Alberta Medical Diagnostic Review Project, starting with the selection of comparison areas; and a description of the Outmigrant Identification for Bias Assessment. The following chapters describe the Crossectional Health Status Evaluation Survey, the Cancer Study, the Birth Defects and Adverse Reproductive Events Study, the Trace Metals Study, the Trace Metals among Hutterites Study, and the Winter Reassessment Study.

The major component of the Southwest Alberta Medical Diagnostic Review Project was a crossectional survey that compared the health status of all eligible residents in the geographically delineated Index (IA) Area with that of samples drawn from two similar areas of Alberta. One comparison area in Alberta was chosen to be as free as possible from any exposure to industrial or man-made contaminants of the environment and sociodemographically comparable to the Index Area (Control Area: Stirling/Raymond - SR); the other was not sociodemographically comparable to the Index Area but was representative of the sociodemographic characteristics of non-metropolitan southern Albertans and was exposed to emissions of sour gas (Control Area: Didsbury-Carstairs-Crossfield-Irricana - DCCI). See map in Figure 2.1/1. We assessed the health indicators of citizens of the three areas in exactly the same way and at the same time of the year (summer 1985). As will be described later we repeated partial determinations in a subsample of the respondents during the winter of 1986 to establish whether there had been any seasonal variation in respiratory signs and symptoms, skin abnormalities, manifestations of allergy, or pulmonary function. We also repeated selected determinations during the late summer in participants studied in early summer to establish whether findings had changed systematically either due to the "learning curve" of the observers and technicians or due to changes in the level of other biologically active agents in the atmosphere.

4.2 Selection of Comparison Areas

4.2.1 Orientation

This section of the report concerns the selection of comparison (control) areas for the Southwest Alberta Medical Diagnostic Review Project. The research design for selecting a sample of residents within each area is described in section 5.1.

4.2.2 Initial Rationale for Selection of Comparison (Control) Areas

Initially, the protocol specified that two areas were to be selected for comparison with the Index Area. These areas were to be defined as:

a) Unexposed Most Comparable Control Area:

As demographically comparable as possible to the Index Area but not exposed to sour gas emissions.

b) Exposed Most Comparable Control Area:

As demographically comparable as possible to the Index Area and exposed to sour gas emissions.

Selection of such areas as controls would allow an evaluation of the effects of both demography and sour gas emissions on the health problems of the Index Area. For example, if health problems were found to be significantly more serious in the Index Area and the Exposed Most Comparable Control Area, than in the Unexposed Most Comparable Control Area, sour gas emission could be considered a potential cause of adverse health effects. Alternatively, if health problems are found to be significantly more serious in both the Index Area and the Unexposed Most Comparable Control Area, than in the Exposed Most Comparable Control Area, demographic characteristics, life style factors and environmental contaminants other than sour gas could be considered potential causes.

In addition to these controls, we expected that by oversampling the non-Mormon population in the Unexposed Most Comparable Control Area, a sufficient sample of "Average Non-Metropolitan Southern Albertans" would remain in that sample to compare with a similar group in the Exposed Most Comparable Control Area, which contained almost no Mormons. Using the groups so assembled the effect of sour gas emissions on the health status of "Average Non-Metropolitan Southern Albertans" could be ascertained.

That was our original plan.

However, as will be noted in later paragraphs of this section, there are no areas in Southern Alberta (south of an east-west line, that runs through Edmonton) that are sufficiently comparable to the Index Area to be properly considered an Exposed "Most Comparable" Control Area. The similarity scores (see section 4.2.8) were simply not low enough in candidate exposed areas to warrant such a designation. Accordingly, we altered the strategy specified in the protocol (with the approval of the Scientific Advisory Board at its meeting with the investigators at Hill Spring in July 1985) such that the choice of the exposed area was to yield a population as similar as possible to the 119 provincial census tracts to the area south of the east-west line running through Edmonton but excluding Calgary and Edmonton since they are metropolitain areas. Thus, the exposed control area is now referred to as the Exposed "Representative" Control Area. The second control area is the most comparable possible Control Area to the Index Area in Southern Alberta with respect to exposure and is also highly representative of the "Average Non-Metropolitan Southern Albertan". Thus, comparisons between the Index Area and the Exposed Representative Control Area are illuminating with respect to any influence which the sociodemographic characteristics of the population of the Index Area might have on the target variables of interest in this project.

4.2.3 Previous Studies

The procedure for selecting comparison areas has been used previously in Ontario in a number of health related studies where the research design required identification of control areas. These studies include:

a) A Study of the Health Status of Residents of the Junction Triangle, Toronto (W.O. Spitzer for the City of Toronto Department of Public Health, 1984). (The demography/geography consultant, R.W. Murdie.)

b) Junction Triangle Health Assessment Program (City of Toronto Department of Public Health, 1985). (Consultant, R.W. Murdie.)

c) Junction Triangle Historical Cohort Cancer Study (City of Toronto Department of Public Health, 1985). (Consultant, R.W. Murdie.)

d) A Community Health Study of the Residents of Whitchurch-Stouffville (Ministry of Health, Province of Ontario, 1985). (Consultant, R.W. Murdie.)

Of these studies, the first (A Study of the Health Status of Residents of the Junction Triangle, Toronto) is most relevant here because it is the only study of the four for which it is possible at the present time to evaluate the reliability of the procedure. The Junction Triangle study required the selection of a comparison census tract in the City of Toronto that was demographically similar to the Junction Triangle but, in contrast to the Junction Triangle, minimally exposed to industry. The results from the questionnaires that were administered to a sample of residents in both the Junction Triangle and the comparison census tract revealed a close correspondence between the areas in terms of demographic composition (Spitzer, 1984). The only major difference between the two areas was in ethnic makeup with Portuguese rather than Italian being the major non-Anglo-Saxon group in one of the tracts compared. However, these differences had been expected beforehand and it was subsequently confirmed that they did not prejudice the reliability of the research results.

4.2.4 Selection of Variables to Derive Demographic Similarity

Evaluation of demographic similarity was based on twelve variables selected from the 1981 Census of Canada. These represented a wide range of demographic characteristics including age structure, family size, mobility, income, educational achievement, occupational status, and religion (Table 4.2/1). In total, it was assumed that the twelve variables selected would provide a comprehensive demographic summary of residents in the Index Area and would serve to differentiate this area from other non-metropolitan areas in Southern Alberta. Because of the relatively large Mormon population in the Index Area, and because of the likelihood that smoking and other health-related practices are substantially desined by religious affiliation, religion was deemed to be a particularly important variable for comparison with other parts of Alberta. Unfortunately, Mormon religion was not available by enumeration area for 1981 and therefore was not included in the formal analysis (1). Mormon religion was available, however, by provincial census tract for 1971 and this information was used to supplement the main analysis.

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(1) In 1981 Mormons were coded by Statistics Canada as "No Religion" and in 1971 as Other Protestant on the enumeration area tapes.

TABLE 4.2/1

VARIABLES INCLUDED IN THE ANALYSIS, 1981 CENSUS

SHORTENED NAME	FULL DESCRIPTION
Pop 0 to 4	Percent population 0 to 4 years of age
Pop 5 to 14	Percent population 5 to 14 years of age
Pop 65+	Percent population 65 years of age and over
6+ Families	Percent families with 6 or more persons
X Income	Average household income
Low Educ	Percent population 15 years of age and over not attending school with primary education only
Some Univ	Percent population 15 years of age and over not attending school with some post secondary education
Farmers	Percent total labour force engaged in farming
Primary	Percent total labour force engaged in primary occupations (other than farming)
United Church	Percent population United Church religion
Catholic	Percent population Catholic religion
Occup $\leq$ 2 yrs	Percent private households occupying present house for two years or less
Mormon, 1971	Percent population Mormon religion, 1971 census

4.2.5 Definition of Benchmark Area

The Index Area, as defined by the ADRP for the Medical Diagnostic Review Project, does not correspond exactly with any enumeration area or census subdivision boundaries. Enumeration areas are the smallest areas used by Statistics Canada for collecting census data. For this reason, a Benchmark Area was defined as the most similar aggregate of enumeration areas that corresponded spatially with the Index Area (1). Although slightly larger in areal extent and population size there is no reason to believe that the Benchmark Area is not similar demographically to the Index Area (2).

4.2.6 Spatial Units of Analysis

As mentioned above, the enumeration area is the smallest data collection unit employed by Statistics Canada. With populations ranging from less than 100 to over 1,000 enumeration areas were considered too small on average and too variable in population size for identifying comparison areas. Instead, it was decided to aggregate the enumeration area data to the level of provincial census tracts. The latter generally have 3,000 to 8,000 people (average = 5,000) and follow well recognized natural or man-made physical boundaries. For this analysis the major advantage of provincial census tracts is their relative spatial compactness and uniform population size. It should be noted, however, that census tracts, like all spatial aggregations, often display considerable intra-area variability, both physically and demographically. For this reason they were used as a first approximation for identifying comparison areas. As mentioned in section 4.2.10.2 further refinements were made to the research strategy particularly for identifying comparison areas exposed to sour gas.

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(1) The Benchmark Area included enumeration areas 254, 255, 257, 261 to 263 and 351 to 354 all in electoral district 814.

(2) The estimated population for the Index Area in 1981 was 2228 whereas in 1981 the census population for the Benchmark Area was 2827.

4.2.7 Geographic Coverage

The search space for comparison areas was restricted to the area south of an east-west line running through Edmonton but excluding the Calgary and Edmonton census metropolitan areas. Also, as requested by Environment Alberta after initial discussions with ADRP project officers, Indian reservations and Hutterite Colonies were deleted from consideration. Excluding the Benchmark Area, 119 provincial census tracts were included in the analysis.

4.2.8 Demographic Similarity

The method for identifying comparison areas is part of a procedure used in taxonomic or grouping analysis and adopted by disciplines in both the physical and social sciences. Much of the early work was in biology (summarized in Sokal and Sneath, 1963) and psychology (e.g., Cronbach and Gleser, 1953) but there are now examples in fields such as geography (e.g., Berry, 1967; Spence and Taylor, 1970) and marketing (e.g., Green et. al., 1967).

The basic objective of these studies is to classify objects (e.g., skulls, tree leaves, individuals, cities, areas within cities, areas within provinces) on the basis of a set of relevant characteristics (e.g., length, width, shape, size, personality traits, economic structure, age of population, ethnicity, occupational status).

Although many distance and classification procedures are available, the most commonly used is the step-wise or hierarchical grouping technique developed by Ward (1963) and operationalized for the computer by Veldman (1967, pp. 108-17).

Examples of the use of the procedure in geography include classifications of Canadian cities (King, 1966; Ray and Murdie, 1972), socio-economic regionalization of census subdivisions in Ontario and Quebec (Berry and Ray, 1966) and classifications of census tracts in Calgary (Davies, 1975) and Edmonton (Davies, 1978).

The indicator of similarity among two or more communities or populations is expressed in a social distance score where the possible values start with the lowest score of 0 (denoting perfect similarity) to very high values. In our experience social distance scores higher than 20 render the communities or populations impossible to compare even with statistical adjustments. Social distance scores under 15 are workable; those under 10 easily handled with adjustments. Scores under 4 permit comparisons without statistical adjustments.

The basic steps in the procedure are as follows:

a) Compute distance (D^2) as a measure of similarity between observations (see details Diagram 4.2/1). The result is a matrix of D^2 values.

b) Identify the pair of observations for which distance (D^2) is minimized and combine into a single group.

c) Replace the columns and rows of these two observations in the D^2 matrix by a single joint column and row in which the average distance (D^2) of the two observations to all other observations is recorded.

d) Repeat (b) and (c) until only one group containing all observations in the data set remains.

e) Theoretically, any number of groups from 1 to N can be selected. One seeks to select a level of grouping where the between group variance is minimized. The optimal number of groups is arbritrary but is usually guided by a measure of within group variation (squared deviation from group means). Ideally, a level of grouping should be selected prior to the point where the within group variation increases markedly in value.

Since the objective of this analysis was not to identify groups of demographically similar census tracts but rather to compare the Benchmark Area with the other 119 provincial census tracts, interpretation of results focused on the D^2 values. The usual method for computing distances in the grouping procedure involves using the Pythagorean Theorem (the square of the hypotenuse of a right angled triangle is equal to the sum of the squares of the other two sides). More generally, the squared distance between two observations and any number of characteristics can be determined using the following algorithm (after Johnston, 1978, p. 215).

Diagram 4.2/1

$$D^2_{ij} = \sum_{k=1}^{n} (X_{ik} - X_{jk})^2$$

where: X_{ik}, X_{jk} are the values for observations i and j on variable k;

n is the number of characteristics or variables; and

D^2_{ij} is the squared distance separating observations i and j.

Lest one be left with the impression that there is unanimity amongst researchers concerning the procedure outlined above it should be pointed out that there is no agreement on a "best" procedure. Ward's (1963) algorithm has probably been used more frequently because of the wide availability of the HGROUP computer programme (Veldman, 1967, pp. 308-17) and its relative ease of use. There are, however, numerous methodological and technical issues in the application of grouping analysis. Three are worth mentioning in relation to the present analysis.

1) Measure of Similarity

For the present analysis the D^2 measure described above was used. In addition to "distance", however, a number of measures have been suggested for measuring similarity including correlations between observations (Sokal and Sneath, 1963). With the distance measure itself, controversy concerns the use of D or D^2. The argument for using D instead of D^2 is that by using the latter large differences between observations are exaggerated. For the purpose of this analysis it is doubtful whether there is a better measure of similarity than distance and the controversy over using D or D^2 is irrelevant since the ultimate purpose is to rank provincial census tracts according to their similarity with the Benchmark Area. Nevertheless, these observations should be kept in mind when interpreting the similarity or D^2 scores in Table 4.2/4.

2) Scale

For this analysis the twelve variables listed in Table 4.2/1 were standardized using Z scores (mean + 0, variance = 1.0) in order to give each characteristic the same importance in the analysis. This seems reasonable when, as in this study, variables are expressed in different units of measurement (e.g., percent population 0 to 4 years of age and average household income) and display quite different means and variances (e.g., percent total labour force engaged in farming - X = 20.5% and S = 282.2% - and percent total labour force engaged in primary occupations other than farming - X - 2.7% and S = 5.8%) Johnston (1970, p. 300), however, has argued that depending on the values of the means and variances there may be situations where the results are quite different from expectations based on the non-standardized data. For this analysis, the general effect of standardization should be kept in mind when interpreting the results.

3) Orthogonality

In this analysis the first twelve variables from Table 4.2/1 were used in standardized form to compute D^2. Many researchers (e.g., Johnston, 1978, p. 217) argue that since the Pythagorean theorem applies to right-angled triangles, the variables used in the calculation of distance measures should be orthogonal or uncorrelated with each other. A common method of achieving orthogonality is to use scores from a principal components or factor analysis of the data as input to the distance calculations. Other authors (e.g., Cronbach and Gleser, 1953, p. 468; Sokal, 1961, p. 75) see no objection to using correlated variables. Intuitively, this position would seem to be justifiable if the correlations between variables are not excessive (excessive defined as outside the range 0.8 or -0.8).

The troubling issue here is double counting. It could be argued, for example, that if measures of income, occupational status and educational achievement are all relatively highly related and included in an analysis, the concept of economic status gets counted three times. Conversely, it could be argued that each of these variables is conceptually independent and all three should be included in an analysis as individual variables. In more practical terms we have found relatively little difference between the results from grouping studies based on the original variables and on an orthogonal transformation of the variables when using groups of highly correlated variables for census tracts in Metropolitan Toronto.

In this study, none of the possible 66 correlation coefficients exceeded +0.8 or were less than -0.8 and all but 14 were between +0.5 and -0.5. It may be assured, therefore, that double counting is unlikely to be a major problem. If more time had been available further experimentation would have been undertaken using the scores from a principal components analysis as input to the distance algorithm. Past experience, however, suggests that the results would not have differed dramatically from those obtained here.

In sum, similarity scores of social distance were computed between the Benchmark Area and all other Provincial Census Tracts for Alberta south of Edmonton using twelve census variables and a modification of programme HGROUP (Veldman, 1967, pp. 314-5) In effect, these scores are measures of social distance between the Benchmark Area and Provincial Census Tracts. The smaller the value, the more similar the census tract with similarity scores less than 15.0 were mapped and rank ordered from lowest to highest. These accounted for approximately one-quarter of the census tracts in the analysis. The similarity score is a descriptive measure for which there is no test of statistical significance.

4.2.9 Sour Gas Plants

The location of sour gas plants in Alberta was derived from a number of sources including:

a) Alberta, Energy and Natural Resources, Provincial Base Map, 1:500,000, 1982;

b) Alberta Environment, Pollution Control Division, Industrial Sulphur Emissions for Alberta, 1977-1981;

c) Delta Projects Limited, Alberta B.C. Gas Plant Map, Jan. 1, 1985;

d) Energy Resources Conservation Board, Map of Designated Oil and Gas Fields, 1985;

e) Energy Resources Conservation Board, Inventory of Gas Processing Plants in Alberta, May, 1985.

No attempt was made to categorize plants by characteristics such as size, emissions, date of construction and emission controls. An attempt was made, however, when refining the search for control areas with sour gas to take into account the predicted areas of deposition surrounding each plant based on prevailing wind direction and height of stack.

4.2.10 General Results

4.2.10.1 Characteristics of the Benchmark Area

Compared to all Provincial Census Tracts included in the analysis, the Benchmark Area (Area 1 in Table 4.2/2) has a considerably younger population, a much larger family size, a higher proportion of persons with university training, a much higher proportion of agricultural workers and a less mobile population. It enjoys about the same income as the average tract and has an average proportion of persons with low educational achievement. It has dramatically lower proportions of United Church adherents and Catholics than the average and a very high proportion of Mormons.

It should also be noted the Benchmark Area is not homogeneous. When the area was divided into two sections, east of the Waterton River (Area 3 in Table 4.2/3) and west of the Waterton River (Area 4 in Table 4.2/3) a number of contrasts were noted, especially concerning religion and economic status. Based on 1971 Enumeration area figures, Mormons, identified by the category Other Protestant, were much more prevalent east of the Waterton River. Also, in 1981 income on average was lower east of the Waterton River (especially in Glenwood and Hill Spring) but educational achievement was higher.

4.2 10.2 Areas Demographically Similar to the Benchmark Area

The Provincial Census Tracts that are most similar demographically to the Benchmark Area extend north to Fort MacLeod, east to Taber and Vauxhall and south to the Montana border (Table 4.2/4). All are relatively close to the Index

TABLE 4.2/2

DESCRIPTIVE STATISTICS

VARIABLES	AREA 1/ ALL EA'S	$\overline{X}$/ALL PCT'S IN STUDY	Sd/ALL PCT'S IN STUDY	MINIMUM VALUE	MAXIMUM VALUE
Pop 0 to 4	11.3	8.6	1.9	3.9	13.4
Pop 5 to 14	21.9	16.8	3.0	7.4	22.7
Pop 65+	7.8	10.2	4.5	1.7	24.7
% Families 6+ Persons	17.2	6.1	3.4	1.1	19.1
Average Household Income	$24,555	25,520	4,815	16,049	54,167
Low Educ	18.3	18.6	6.7	4.4	38.8
Some Univ	15.6	11.9	4.6	2.4	34.1
Farmers	50.0	20.5	16.8	0.6	58.8
Primary Occup	0.75	2.7	2.4	0.0	12.9
United Church	10.7	27.0	8.4	7.1	50.3
Catholic	11.6	21.3	7.7	0.9	44.8
Occup $\leq$ 2 yrs	26.6	37.1	10.3	15.5	73.7
Mormon, 1971	40.7	3.4	7.4	0	54.6

TABLE 4.2/3

CHARACTERISTICS OF THE BENCHMARK SUBAREAS

VARIABLES	$\bar{X}$/ALL PCT'S IN STUDY	AREA 1 ALL EA'S	AREA 2 ALL EA'S EXCEPT 354*	AREA 3 EA'S EAST OF WATERTON RIVER	AREA 4 EA'S WEST OF WATERTON RIVER
Pop 0 to 4	8.6	11.3	11.7	13.3	8.8
Pop 5 to 14	16.8	21.9	21.9	22.5	21.2
Pop 65+	10.2	7.8	8.0	9.2	6.0
% Families 6+ Persons	6.1	17.2	17.9	19.1	14.8
Average Household Income	$25,520	24,555	22,288	20,130	30,266
Low Educ	18.6	18.3	16.7	15.1	22.7
Some Univ	11.9	15.6	16.0	19.4	10.6
Farmers	20.5	50.0	50.2	53.2	46.5
Primary Occup	2.7	0.75	0.9	0.7	0.8
United Church	27.0	10.7	10.1	7.1	15.5
Catholic	21.3	11.6	8.7	0.9	25.4
Occup ≤ 2 yrs	37.1	26.6	28.7	28.0	24.6
Mormon, 1971**	3.4	40.7	45.5	71.2	15.0

* Mennonite/Hutterite in EA 354 (1971) = 20.7%

** Defined as "no religion" except X

TABLE 4.2/4

PROVINCIAL CENSUS TRACTS MOST SIMILAR DEMOGRAPHICALLY TO THE BENCHMARK AREA (RANK ORDERED)

SEQ NO.	PCT	SOCIAL DISTANCE "SIMILARITY SCORE"	GENERAL LOCATION	SEQ NO.	PCT	SOCIAL DISTANCE "SIMILARITY SCORE"	GENERAL LOCATION
15	7008	1.4	Stirling, Raymond	13	7006	12.0	Milk River, Coutts
36	7026	2.6	Barnwell, Taber, Vauxhall	99	7163	12.4	Edberg, Rosalind
16	7009	3.2	Cardston	40	7030	13.0	Vulcan, Milo, Lomond
14	7007	3.6	Magrath, Warner	38	7028	12.7	Redcliff
46	7035	5.1	Cluny, Hussar	21	7014	18.3	Fort MacLeod
47	7036	8.5	Bassano, Duchess	69	7134	13.2	Clive
23	7015.01	8.7	Coalhurst	96	7160	13.3	Beaumont, Leduc
34	7024	9.5	Coaldale	45	7034	13.5	Gleichen
37	7027	9.9	Bow Island, Burdett	93	7158	13.5	Calmar, Devon, Leduc
20	7013	10.8	Cowley north to Longview	82	7147	13.6	Bentley, Eckville
112	7176	10.9	Tofield	64	7129	13.8	Coronation, Veteran
52	7041	11.7	Carbon, Linden, Rockyford	12	7005	14.1	Irvine, Medicine Hat
98	7162	11.7	Millet, Wetaskiwin	51	7040	14.2	Munson, Drumheller
106	7170	11.8	Dewberry	62	7127	14.6	Three Hills, Trochu

Area. This is simply a reflection of Alberta's physical, economic and cultural geography. Beyond this, broad sectors of demographically similar tracts extend east from Lethbridge through Bow Island to Medicine Hat and north from Lethbridge through Vulcan, Gleichen/Bassano, Drumheller and Leduc to Edmonton. When compared to the location of sour gas plants the areas identified as demographically similar to the Benchmark Area allow ample choice of an Unexposed Control Area. However, identification of the most suitable exposed comparable control area was difficult. Indeed, the areas identified above as demographically similar to the Benchmark Area and the areas exposed to emissions from sour gas plants are spatially independent of each other. More specifically, the scores for areas most demographically similar to the Benchmark Area and exposed to sour gas are minimally in the 15 to 20 range as compared to scores of less than 4 for areas that are demographically similar and not exposed. Even accepting the caveat that these are D^2 as compared to D scores, the difference between the two sets of scores is quite substantial. Given these circumstances, all areas with sour gas plants between Twin Butte and Edmonton were evaluated using demographic data by enumeration areas. In addition, a field check of these areas was made by the senior geographic consultant (Dr. R.A. Murdie) and/or Dr. Dennis Stokes, Senior Research Manager, Research Management Division, Alberta Environment. It was concluded that a similarity and exposed area did not exist.

4.2.11 Final Choice of Comparison Areas

4.2.11.1 Unexposed Most Similar Control Area

The four census tracts that are most similar demographically to the Benchmark Area are the best candidates (Table 4.2/4). All have a relatively high proportion of Mormons (1971) although what evidence is available suggests that the Stirling/Raymond (SR) area comes closest to matching the Benchmark Area (Table 4.2/5). The Cardston area has a higher proportion of Mormons and Barnwell/Taber and McGrath/Warner a lower proportion of Mormons. Otherwise, all four areas closely approximate the Benchmark Area. Although the areas are ranked below in preferred order, there is little to choose between them. Since Pincher Creek had been excluded from the Index Area, it was decided that the major towns in each of these areas should also be excluded from consideration.

TABLE 4.2/5
CANDIDATE AREAS WITH > 10% MORMON POPULATION AND NOT EXPOSED TO SOUR GAS

			(1)	(2)	(3)	(4)
VARIABLES	$\overline{X}$/ALL PCT'S IN STUDY	AREA 1 ALL EA'S	CT 7008 STIRLING/ RAYMOND	CT 7026 BARNWELL TABER, ETC.	CT 7009 CARDSTON	CT 7007 McGRATH WARNER
Pop 0 to 4	8.6	11.3	12.8	10.1	10.8	11.1
Pop 5 to 14	16.8	21.9	22.3	20.7	20.6	20.2
Pop 65+	10.2	7.8	9.0	7.2	13.0	9.6
% Families 6+ Persons	6.1	17.2	16.1	17.1	15.9	11.9
Average Household Income	$25,520	24,555	22,935	25,011	22,562	22,341
Low Educ	18.6	18.3	21.0	21.7	15.0	29.8
Some Univ	11.9	15.6	15.2	14.3	20.4	13.1
Farmers	20.5	50.0	29.7	40.3	25.4	47.0
Primary Occup	2.7	0.75	0	2.38	0.89	0.25
United Church	27.0	10.7	7.5	22.7	7.3	16.6
Catholic	21.3	11.6	11.0	20.6	6.6	9.8
Occup $\leq$ 2 yrs.	37.1	26.6	28.5	27.3	32.0	23.1
Mormon, 1971	3.4	40.7	41.6	20.4	54.6	28.2
Population, 1981		2,827	5,501	4,737	5,392	4,850
Social Distance "Score"			1.4	2.6	3.2	3.6

CT = Census Tract

a) Stirling/Raymond Area (Census Tract 7008):

With the exclusion of Raymond, slightly lower than the Benchmark Area in respect of young children and university educated residents but otherwise similar demographically; no known source of industrial pollution; relatively compact spatially; within commuting distance of the Index Area.

b) Barnwell/Taber/Vauxhall Area (Census Tract 7026):

Fewer Mormons than the Benchmark Area; Turin gas plant lies just west of this area - no sulphur recovery but sulphur emissions measurable within one mile of the plant; relatively compact spatially; not within easy commuting distance of the Index Area.

c) Cardston Area (Census Tract 7009):

High proportion of Mormons; otherwise demographically similar to the Benchmark Area; no known source of industrial pollution; relatively compact spatially; adjacent to the Index Area - may have high level of in-migration from Index Area.

d) McGrath/Warner Area (Census Tract 7007):

Fewer Mormons than the Benchmark Area; considerable demographic variation within tract variation demographically; no known source of industrial pollution; not as compact spatially as the Index Area.

4.2.11.2 Exposed Representative Control Area

As noted in section 2.2 and section 4.2.10.2, identification of areas that are demographically similar to the Index Area and exposed to sour gas emissions do not exist. With respect to emissions, from information supplied by Alberta Environment, it was determined that several areas near Calgary closely approximated the predicted range of deposition known to affect the Index Area (IA).

The five candidate areas listed below are thus deemed to be the most suitable from the standpoint of exposure although none approximate the Benchmark Area demographically as well as the areas identified in section 4.2.11.1. All have a much higher proportion of non-Mormon religion, dramatically smaller family size and fewer children than the Benchmark Area. These areas also differ in economic status according to their proximity to Calgary. As noted below, areas within fifteen miles of the

Calgary census metropolitan area generally have a higher socio-economic status and lower farm population than areas further away from Calgary. This is particularly characteristic of areas to the south and west of the city. This factor has influenced the ranking of candidate areas. Estimates of the demographic characteristics for these areas based on the averages for enumeration areas within the predicted areas of deposition are shown in Table 4.2/6. In the table, the areas are ordered in terms of preference as listed below. All are within daily commuting range of Calgary but there seems to be considerable variation in the influence that urban to rural migration has had on these areas with Okotoks most affected and the Lone Pine Creek area least affected. This is particularly evident for variables related to income, educational achievement, farm population, and recency of occupance. That is, the Okotoks area has a much more affluent, highly educated, non-farm, and less stable population than the area surrounding Lone Pine Creek.

a) Area Surrounding the Lone Pine Creek Plants (Canadian Superior and Dome) east of Carstairs

Includes area ten miles north, east, and south of the plants; aside from the characteristics noted above similar to the Benchmark Area except lower on educational achievement; relatively little within area variability in population;

TABLE 4.2/6

CANDIDATE AREAS; TO SELECT AN EXPOSED REPRESENTATIVE CONTROL AREA
(%)

VARIABLES	$\overline{X}$/ALL PCT'S IN STUDY	BENCHMARK AREA	PINE CREEK (CAN SUP DOME)	CARSTAIRS/ CROSSFIELD (HOME)	CROSSFIELD EAST (AMOCO)	CROSSFIELD (CAN OCCIDENTAL)	OKOTOKS (KIDD CREEK)
Pop 0 - 4	8.6	11.3	9.8*	7.3*	7.7*	7.3*	6.5*
Pop 5 - 14	16.8	21.9	17.4	14.9	18.1	20.3	16.9
Pop 65+	10.2	7.8	7.0	8.0	5.8	4.7	6.6
% Families 6+ Persons	6.1	17.2	5.3	1.5	4.6	6.7	4.6
Average Household Income	$25,500	24,555	25,211	26,142	31,650	36,888	37,923
Low Educ	18.6	18.3	17.8	15.5	14.1	12.2	8.3
Some Univ	11.9	15.6	7.8	13.6	11.4	14.8	17.4
Farmers	20.5	50.0	61.5	46.4	41.7	26.1	22.9
Primary Occup	2.7	0.75	0.2	1.8	0.3	0	1.6
United Church	27.0	10.7	26.8	30.7	35.2	34.7	39.1
Catholic	21.3	11.6	18.4	12.6	15.4	22.3	16.1
Occup ≤ 2 yrs	37.1	26.6	17.4	26.2	25.5	29.9	29.1

* All figures in these columns based on "crude averages" (sum of figures for enumeration areas within the predicted areas of deposition divided by the number of enumeration areas).

Mennonite population (unknown number) may have to be accounted for; topographically similar to the Index Area including presence of coulees - may be important because of apparent variation of exposure to sour gas emission with height of land in the index area.

b) Area Surrounding the Carstairs/Crossfield Plant (Home) West of Carstairs

Includes area ten miles north, east, and south of the plant; population in the southern part of this area also affected by the Amoco plant at Crossfield East; aside from characteristics noted above similar demographically to the Benchmark Area; relatively little within-area variability in population characteristics.

c) Area Surrounding the Crossfield East Plant (Amoco) South of Crossfield

Includes area ten miles north, east, and south of the plant; higher income than the Benchmark Area; considerable variation within the area - much higher income in the vicinity of Highway 2 between Airdrie and Crossfield; area also affected by the Home plant to the north and the Canadian Occidental plant to the south.

d) Area Surrounding the Crossfield East Plant (Canadian Occidental) south of Airdrie

Includes area up to twenty miles north, east, and south of the plant; much higher incomes and lower farming population than the Benchmark Area within ten miles of the plant; considerable within-area demographic variation; northern part of the area also affected by the Amoco plant.

e) Area Surrounding the Okotoks Plant (Kidd Creek) East of Okotoks

Includes area up to ten miles north, east, and south of the plant; excluding the Town of Okotoks, the area is much higher than the Benchmark Area in income and educational achievement; much lower in farmers than the Benchmark Area; considerable within area demographic variation; area to the north of the plant towards Calgary has a much higher economic status.

4.2.11.3 Combined Exposed Representative Area

The four exposed representative control areas north of Calgary that were identified in the previous section are all relatively close to each other and in some cases their predicted areas of sour gas deposition overlap. Given this situation, it was decided to combine these areas into a single spatial unit and evaluate the similarity of this unit to the Benchmark Area, the preferred Unexposed Representative Area (Stirling/Raymond) and the mean value for all Provincial Census Tracts in the study.

Because of uncertainty about the extent of deposition from the Crossfield East Plant (Canadian Occidental) two variations of the combined area were identified.

a) Area north of Calgary surrounding the Lone Pine Creek Plants (Canadian Superior and Dome), the Carstairs/Crossfield Plant (Dome), the Crossfield East Plant (Amoco) and the Crossfield East Plant (Canadian Occidental) excluding the town of Airdrie. Airdrie was excluded because it increased about sixfold in population between 1976 and 1981 and would appear to have become primarily a dormitory town for Calgary rather than a rural service centre like the smaller towns in southwest Alberta.
(Includes Enumeration Areas 310, 313, 314, 315, 320, 351, 365, 403, 407 and 427 in Electoral District 802 and Enumeration Areas 5, 51, 53 to 56, 61 to 63, 66 to 71, 73, 317, 318 and 352 in Electoral District 818).

b) Same area as in (a) above excluding the area southeast of the Canadian Occidental Plant. (Excludes from the list in (a) above Enumeration Areas 313, 315, 320, 402 and 427 in Electoral District 802).

Details concerning the comparisons are provided in Tables 4.2/7 and 4.2/8. There is very little difference demographically between areas (a) and (b). Indeed, the difference in D value is .2 between the two areas thereby indicating that inclusion or exclusion of the area southeast of the Canadian Occidental Plant has virtually no impact demographically in spite of its proximity to Northeast Calgary. Thus, the remainder of the discussion will refer only to area (a) - the entire area north of Calgary excluding Airdrie, which was chosen to become the Exposed Representative Area.

Table 4.2/8 shows that the area north of Calgary selected is not very similar demographically to the Benchmark Area, thereby substantiating the more general conclusions in section 2 and section 4.2.10.2. The D^2 value of approximately 15 is similar to similarity scores obtained earlier for exposed areas most similar demographically to the Benchmark Area. Put another way, the area north of Calgary was the 19th most similar area to the Benchmark Area out of the 120 included in the study (119 Provincial Census Tracts and the combined area north of Calgary). More specifically as indicated in Table 4.2/7, the area north of Calgary differs from the Benchmark Area in that it has fewer children, smaller families, a much different religious makeup, relatively speaking a much larger number of recently arrived families and a slightly more affluent population.

Of particular interest from Table 4.2/8 is the observation that the combined area is very close demographically to the average for all Provincial Census Tracts included in the analysis. This justifies our designation of this control group as the Exposed Representative Area. Thus we had a sample of "Exposed Average Non-Metropolitan Southern Albertans" to compare with a sub-sample selected from the people in the Unexposed Most Similar Area of Stirling/Raymond by excluding Mormons of that area in many of the comparisons done in the analysis. The subsample abbreviated as SR-M was a control group characterized as "Unexposed Average Non-Metropolitan Southern Albertans".

TABLE 4.2/7

CHARACTERISTICS OF SELECTED REPRESENTATIVE AREAS (%)

VARIABLES	$\overline{X}$/ALL PCT'S IN STUDY	BENCH-MARK AREA	STIRLING/ RAYMOND AREA	AREA NORTH OF CALGARY EXCLUD. AIRDRIE (DCCI)	AREA NORTH OF CALGARY EXCLUDING AIRDRIE AND AREA SE OF THE CAN. OCCIDENTAL PLANT
Pop 0 to 4	8.6	11.3	12.8	8.8	9.4
Pop 5 to 14	16.8	21.9	22.3	18.4	18.2
Pop 65+	10.2	7.8	9.0	7.6	9.0
% Families 6+ Persons	6.1	17.2	16.1	4.8	4.4
Average Household Income	$25,520	24,555	22,935	27,540	26,164
Low Educ	18.6	18.3	21.0	14.2	15.6
Some Univ	11.9	15.6	15.2	12.4	11.5
Farmers	20.5	50.0	29.7	23.1	25.5
Primary Occup	2.7	0.75	0.0	1.7	2.2
United Church	27.0	10.7	7.5	31.3	31.5
Catholic	21.3	11.6	11.0	18.1	16.9
Occup $\leq$ 2 yrs	37.1	26.6	28.5	35.1	35.6
TOTAL POP		2827	5501	15758	11294
TOTAL HOUSEHOLDS		722	1426	4848	3515

TABLE 4.2/8

SELECTED SOCIAL DISTANCE SIMILARITY SCORES

AVERAGE* vs.	SIM. SCORE	BENCHMARK AREA vs.	SIM. SCORE	STIRLING/ RAYMOND AREA vs.	SIM. SCORE
1. Benchmark Area	14.1	1. Stirling/ Raymond	1.4	1. Area north of Calgary excluding Airdrie	15.5
2. Benchmark Area east of the Waterton River	24.5	2. Area north of Calgary excluding Airdrie	14.8	2. Area north of Calgary exluding Airdrie and the area SE of the Can. Occidental plant (dashed line on the master map)	15.1
3. Benchmark Area west of the Waterton River	9.3	3. Area north of Calgary excluding Airdrie and the area SE of the Can. Occidental plant (dashed line on master map)	14.7		
4. Stirling/ Raymond Area	14.2				
5. Area north of Calgary excluding Airdrie	1.1				
6. Area north of Calgary exclud. Airdrie and the area SE of the Can. Occidental plant (dashed line on the master map)	.9				

* Average = average for all provincial census tracts south of an east-west line through Edmonton but excluding the Edmonton and Calgary census metropolitan areas.

4.2.12 Comment

The objective of this process was to select two comparison areas. Given the non-existence of exposed citizens similar to Index Area, we decided upon an Unexposed Most Similar Control Area and an Exposed Representative Area. The first control area was for the main comparisons with the Twin Butte Index Area. The additional control area permitted assessments of the effect of exposure on representative Albertans in the rural south of the province. Measurement of demographic similarity was based on 1981 Census of Canada data and the calculation of social distance similarity scores between the Index Area and the other 119 Provincial Census Tracts included in the analysis. Information concerning sour gas and other industrial pollution was obtained from Alberta Environment.

The results suggest a clearcut choice for the Unexposed Most Similar Control Area with the Stirling/Raymond-Taber-Vauxhall, Cardston and McGrath/Warner in that order. Fortunately, the people of Stirling/Raymond, who had the lowest social distance similarity score, indeed the lowest, accepted the role of principal control community. For a variety of reasons, selection of an Exposed "Most Similar" Control Area was not feasible. The basic problem was that no other area in Alberta south of Edmonton with sour gas contamination is sufficiently similar demographically to the Index Area. This is primarily due to the unique cultural characteristics of the Index Area and adjacent parts of Southern Alberta -- a relatively high proportion of Mormons and associated characteristics of large family size and high educational achievment. Thus, with approval of the Scientific Advisory Board at the site visit at Hill Spring in July 1985, the plan changed to select an area most representative of all Southern non-Metropolitan Albertans from the 119 Provincial Census Tracts analyzed in this process. An Exposed "Representative" Control Census Area emerged. Of the various alternatives, an enlarged area surrounding several gas plants north of Calgary (which excluded the City of Airdrie) was judged to be the most suitable.

The demographic data on which this study was based were collected by Statistics Canada in June, 1981. Thus there was a four-year time lag between the census and the Medical Diagnostic Review field work. Given that an average of twenty percent of North American households move every year (Short, 1978), the potential for a change in area characteristics is great. The relationship between residential mobility and demographic structure is complex. While there has probably been little change over the past few years in the demographic structure of the Benchmark Area and the Stirling/Raymond Area, the possible further movement of a relatively young urban-oriented population into the semi-rural area north of Calgary between 1981 and 1985 may have accentuated the differences between this area and the Benchmark Area. In the Calgary area, assessments of change during the past four years are further complicated by the volatility of the housing market. Specific details about possible impacts on demographic structure are not yet available. However, the "proof of the pudding" about correct selection of comparison areas is the actual distribution of relevant sociodemographic variables in the samples drawn for the study. The data showing whether our methods for selecting control areas worked or not are given later under Methodological Results in sections that describe the samples of our respondents.

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4.3 Outmigrant Identification for Bias Assessment

4.3.1 Introduction

Positive identification of outmigrants and documentation of their health is essential for determining whether there was biased selective outmigration due to health reasons among the three areas; that is, to determine whether the comparisons of health status between the three areas could have been affected by the movement of more healthy or more sick people out of one or other area in a systematic way. If so, the addition of outmigrant data could allow corrections or judicious interpretation of findings. Also outmigrant data will be helpful as a means of expanding the follow-up experience to be used in the contrasts of incidence rates.

The ascertainment and counting of those who moved away or died between 1957 and 1985 permits the completion of the list of individuals who have resided in the Index and control areas during this time. In this project, all the individuals who either died or moved away from their area are called "outmigrants". This "outmigrant" component is distinct from the main study in field tactics and procedures of execution, but has been planned to be complementary in analysis and interpretation. Data collection procedures were similar among the three areas, particularly regarding the thoroughness of ascertainment and degree of diligence in follow-up. The information provided in this component is useful for the analysis of "health status" in the cancer and in the reproductive studies of this project.

4.3.2 Objectives for the Ascertainment of Outmigrants

The main objective of the search of outmigrants was to obtain health data from former residents that will permit the detection of any differential health-selective outmigration. In addition, the comparison of incidence rates of selected disease and adverse health events among the three study areas complements the data from participants who lived in the study areas as of 1985.

4.3.3 Categories of Information

A select subset of health outcomes was chosen from the *a priori* set of outcome variables employed in the main crossectional component. This subset was established on the basis of relevance to the complaints of the resident population and investigative feasibility. The information collected among outmigrants includes:

a) Readily diagnosed irreversible disease (with emphasis on respiratory and neurological pathology);

b) Other readily diagnosed serious disease, whether reversible or not;

c) Reproductive outcomes and birth defects;

d) Mortality, general and disease specific (all cancers, all respiratory-linked).

Additional categories of information elicited to provide necessary data on potential confounding factors are:

a) Demographic characteristics (date of birth and religion);

b) Residence in study area: date of entry, date of exit, total length of residence in area;

c) Reasons for moving out of the area.

4.3.4 Ascertainment of Outmigrants

The first goal of this research component was to develop an enumeration of outmigrants that was as complete as possible. To this end many sources of information had to be used and the collection of this information involved many steps.

The steps in the development of the enumeration list differ according to the area studied. Indeed, depending on the key outcomes of interest, the reference or control populations differ. For example, in the cancer study, the outcomes of interest are relatively uncommon and this requires large reference populations. For such a comparison, the number of outmigrants should be as large as possible, hence the need to reconstitute the total list of outmigrants in the Index Area.

For the health status evaluation most of the outcomes are more frequent, making less stringent the constraints on the number of outmigrants that have to be available for comparison.

As described in Chapter 5, the entire IA population was studied, whereas in the two control areas random samples of the population were studied. For IA, a complete ascertainment of outmigrants was theoretically possible and this goal was pursued. In the control areas, since only a sample of the population was known, it was impossible to ascertain all outmigrants. Consequently, only immediate outmigrant relatives of the identified sample were pursued (children, siblings and spouse's siblings). In comparisons of outmigrants across the three areas, we used all identified immediate outmigrants, relatives of the control area samples, and a suitably sized sample of all known IA outmigrants.

This explains why the steps taken in the ascertainment of outmigrants in the Index Area will differ from the steps in the control areas. The difference is in the breadth of enumeration or sampling of denominators, not in the effort to ascertain the numerator information used to develop rates for comparison.

4.3.4.1 Development of the Outmigrant List - Index Area

As noted in earlier chapters, the Index Area, as delineated by officials of Alberta Environment, does not correspond to any single or aggregate political or municipal jurisdiction. For example, the Index Area does not lie within any single Municipal District; rather, about 50% of the Index Area lies within the Municipal District of Pincher Creek, about one third of the Index Area lies within the Municipal District of Cardston, and the remainder of the Index Area lies within the Municipal District of Willow Creek. Secondly, because this is a rural area, postal addresses in the Index Area are not described by streets and street numbers as would occur in an urban area; rather, a large proportion of individuals who live or have lived in the Index Area will have as their postal address simply a post office box in the town of Pincher Creek or in the town of Cardston. Thus, for example, if one is searching historical records and finds an individual whose mailing address is a post office box number in Pincher Creek, it is impossible to determine from that record whether the individual resided within the boundaries of the Index Area. For this reason it became apparent at the outset of this study that any historical record based on mailing addresses would be of limited use in enumerating the outmigrants. The only classification system of residents that can be used to determine whether an individual actually resided within the boundaries of the Index Area is the range, township, and section number classification which is used to describe quarter sections of land in this and other areas. This system is used in Alberta rural municipal tax registers and, therefore, we relied on historical municipal tax records in the enumeration process.

Step 1

At the time of the visit to the site for the health evaluation survey, at least one adult member of each household participating in the crossectional survey in the Index Area during the summer of 1985 was asked to complete a form concerning outmigrants. Specifically, they were asked to supply the name, maiden name if applicable, date of birth, year of entry into the Index Area, year of exit from the Index Area, year and cause of death if applicable, current address, and current telephone number, of any friend or relative who had lived within the Index Area and who had moved away or died anytime since 1957. In addition, they were asked to supply similar information for any individuals who were known to have lived in their dwelling before them in the interval since 1957.

Step 2

Throughout the duration of the study in the summer of 1985, interested individuals as well as the Community Advisory Board members continuously supplied lists of outmigrants and their corresponding outmigrant information. These were added to the outmigrant file on a continuing basis.

Step 3

Other potential sources of information about outmigrants were assessed at the outset of the study. The school offices in Cardston were visited and school records for the period 1957-1970 were assessed. These were found to be unacceptable in terms of the quality of the information available. In addition, church records of the local Anglican and Latter Day Saints Churches were also evaluated and unfortunately found to be inadequate for our purposes.

Step 4

During the summer of 1985, a systematic and exhaustive search of tax records was undertaken. Because the Index Area is comprised of portions of 3 distinct municipal districts (Pincher Creek, Cardston, Willow Creek), the process involved multiple visits to the administration offices of these three municipal districts. The land tax record search was conducted as follows: for each individual quarter section of land lying within the boundaries of the Index Area, the tax records for that quarter section were searched as far back as 1957. For each quarter of land, a complete listing of land title holders going back to 1957 was assembled. While computerized lists were available in all three districts for more recent years, a manual search of thousands of land tax records was required to cover the period of interest.

Step 5

Following completion of the comparative health survey in the Index Area, the outmigrant information collected to date was collated in the following manner: for each household in the Index Area, the list of outmigrants and outmigrant information supplied by members of that household was collated with all previous owners of the household property as determined by the land tax record search.

Step 6

A detailed outmigrant information summary package was then designed and assembled for each household in the Index Area. First, information obtained from the household during the visit to the health survey was entered. Second, all previous owners of the household property identified through land tax records were listed separately within the package.

Step 7

A further effort was made to pick up stray omissions. Over approximately a ten day period at the end of August 1985, following completion of the Index Area health survey, a telephone survey of the Index Area was conducted. For over 80% of the

Index Area households, at least one adult member of the household was successfully contacted. During the telephone interview, the interviewee was reminded of the list of outmigrants and the outmigrant information that had been provided by his or her household during the health survey interview. For each listed outmigrant, the outmigrant information was confirmed and/or updated as appropriate. In addition, information was also solicited about additional outmigrants that had not been previously gathered. As well, the interviewee was prompted with the names of all previous owners of his or her property as derived from the land tax record search in an attempt to generate additional names of potential outmigrants. These additional outmigrants, if confirmed, were also added to the file. Any secondary sources of information on reported outmigrants were recorded should these people need to be contacted for more complete information on a particular outmigrant.

Step 8

After telephone survey was completed, all outmigrant information was entered onto a computer data base and sorted alphabetically by surname. This allowed us to consider replication of identification, that is the identification of a potential outmigrant from independent sources. We defined a "singleton" to be a potential outmigrant listed in the outmigrant file for whom there was only one source of identification. For the vast majority of outmigrants, however, several sources named the potential outmigrant. In such cases, typographic disparities were corrected and incongruities in outmigrant information were investigated. At this point, an Outmigrant Review Panel was constituted for each of the five communities. Each panel consisted of two individuals, long-time residents of the area, who were identified by the local Community Advisory Board representative as being most familiar with past residents of their own particular community. Each Outmigrant Review Panel reviewed the list of potential outmigrants along with project research staff in order to verify and/or improve the quality of the information previously assembled. In the case of "singletons" in particular, who by definition had been only identified by one previous source, the Outmigrant Review Panel was asked to confirm the existence of such outmigrants.

Step 9

A high proportion of the residents of the Index Area are members of the Church of Latter Day Saints. Therefore, Bishops of that denomination were asked for assistance in finding ways to contact those outmigrants for whom addresses were missing. Each Bishop returned a computerized list of outmigrant names sent to him for recording addresses obtained from church records or other church members. These lists were also reviewed by other community members.

Step 10

To confirm mortality, the edited outmigrant file was then manually linked to the mortality file supplied by Alberta Vital Statistics. These were microfiches containing all records of mortalities in Alberta from 1961 through April 4, 1985. Each listed outmigrant was checked against the Alberta Mortality File to determine vital status and to determine exact date of death. The outmigrant file was updated as appropriate.

Step 11

While in the Index Area for the winter reassessment during January of 1986, a second telephone effort was made to obtain mailing addresses for those outmigrants we had as yet been unable to contact. Not only were original phone sources re-contacted, but secondary sources were called as well. These were people identified by original sources and also identified through the response from the religious leaders and other community representatives. If these calls led to tertiary sources, every effort was made to contact these people as well for information.

Step 12

After all efforts described previously were completed, a newspaper ad was published containing those names for whom no address had yet been obtained. The newspaper is widely read in the area concerned. This was a final effort in obtaining mailing addresses on the remaining 106 identified outmigrants from the Index Area who had yet to be contacted. Approximately 7% of those listed in the paper were traced in a manner useful to the project.

4.3.4.2 Development of the Outmigrant List - Control Areas

Step 1

Standardized forms were interviewer-administered in the control areas at the time sampled area residents participated in the crossectional survey. It included the same information that was obtained in Steps 1 and 7 for the Index Area.

Step 2

Although control area participants were requested at the time of booking their appointments to be prepared to provide information on outmigrants, many of them did not have all the necessary information at hand during their visit to the study site. In this case, a mail-in form was provided so they could mail the missing information at a later date.

Step 3

Participants were re-contacted by phone in the same manner described under chapter 12 for the Index Area. This was done while in Stirling for the Winter Reassessment (January 1986) and Crossfield participants were re-contacted by our office in Calgary in January and February of 1986.

4.3.5 Handling of the Outmigrant Information

4.3.5.1 Production of the Outmigrant Master List

After all steps were completed in the initial acquisition of outmigrant identities of persons in the field, previously compiled household clusters were coded for data entry. This was done using a standardized format which was developed to accommodate the person-specific information from all the various sources used. This coded information was then entered into a micro-computer data file which had been designed expressly for this purpose. This process resulted in a distinct and separate record for each individual reported. The coding system and standardized format used are included in Appendix 4.3.5.

The list which resulted was sorted alphabetically and printed. This list contained over 8,000 records and was a product of all the information obtained from all efforts and all sources to that point. Many of these 8,000 records were duplicates and therefore an intense editing process took place. It was this hand edited list which was used in the meetings with the Outmigrant Review Panels described in Step 8 previously.

4.3.5.2 Editing of the Outmigrant Master List

This list was to evolve greatly in the next few months. Many changes were the result of additional information obtained as described in Steps 10, 11 and 12 in section 4.3.4.1, and in Steps 2 and 3 in section 4.3.4.2. The list was meticulously edited many times to eliminate duplication. This was done by comparing records to detect duplication of names and verifying this with at least one more piece of information common to those records. This information was usually the outmigants' address or birthdate. Name duplications were sometimes difficult to ascertain because of misspelling or the use of maiden rather than married names. For such reasons the list was subjected to many edits.

After Step 10 in section 4.3.4.1 and Step 3 in section 4.3.4.2 were completed, an edit of "singletons" (who are described in Step 8 in section 4.3.4.1) was done. Singletons without a complete mailing address were deleted. Those with a complete mailing address were sent a questionnaire. If no response was forthcoming, they were deleted from the denominator as well.

A key criterion which determined eligibility of a candidate to be confirmed as an outmigrant required that there be two independent sources giving evidence of the existence of the outmigrant and that he or she in fact lived in one of the three areas during the period of time of concern as specified above. This is analogous to the manner in which banks, airlines, and immigration officers frequently function; they request at least two different types of identity documents before accepting that a person is indeed whom he or she claims to be. Thus, names derived from one source only were deleted from the outmigrant list and not included in the denominators. The lists of people who remained with eligible outmigrant status were identified from at least two sources. Such sources included: a report from a current resident as recorded in data gathering instruments during the summer field survey (1985), appearance in municipal title lists, confirmation from other sources given to us by current residents, a separate report from a different long-term resident member of the Outmigrant Identification Panel, confirmation and/or further information provided by Latter Day Saints Bishops. The bulk of searches, verifications, determinations and confirmations was done manually by a team of research associates, supervising research assistants, and summer students. Whenever there were doubts, a Co-Principal Investigator made the final decision on eligibility.

4.3.6 Data Collection

4.3.6.1 Instruments

Data collection instruments were created to include certain variables also elicited in the questionnaire in the crossectional survey. Items included in these forms as well as the procedures for data collection were identical among the Index and control areas to allow valid comparisons among them. Two types of questionnaires were developed, one for adults and one for children. These were self-administered questionnaires to be sent to and completed by all identified outmigrants from the three areas. These survey instruments were designed to document outmigrants' health status in terms of the key verifiable or "hard" outcomes and potentially confounding variables already identified.

4.3.6.2 Questionnaire Pretest

Ten questionnaires were mailed to ten selected outmigrants from the Index Area in late August. Seven out of these ten questionnaires were returned fully completed. Minor changes were made to the final version of the questionnaire based on this pretest.

4.3.6.3 The Mailout Package

The ascertainment of outmigrants focused on individuals rather than households or families. Therefore, information on household composition was not available at the time of mailing packages. This resulted in the decision to send out standard packages which consisted of two adult and two children questionnaires and a household enumeration form. Information contained on the enumeration form served to identify other members of the household who were also outmigrants and to whom a questionnaire was to be sent.

The first page of the adult questionnaire contains a map of the study area which corresponded to the outmigrant's area of former residence. Respondents were asked to show on this map the location of their former residence. To avoid any possible bias introduced by invalid claims of former residence in the area, these maps contained a larger area than that of interest and did not show the actual boundaries. This strategy although useful in the verification of former residence as part of the eligibility criteria, also led to misunderstandings of what was meant by 'study area'. Therefore, when a misunderstanding of this sort was suspected, ascertainment sources were assessed according to their degree of reliability in order to make a final decision on eligibility. These cases were flagged with a specific status code and a sensitivity analysis was done to determine the effect of inclusion or exclusion of this data.

The mailout package also contained a covering letter explaining the purpose of the study and instructions on how to complete the questionnaires. In order to facilitate prompt and efficient return of completed questionnaires a "Business Reply Mail" envelope was enclosed.

4.3.6.4 Mailout Logistics

A logging system was developed in order to handle the mailout questionnaires properly and to monitor the return. A mailout log was used to record serial numbers by area and to monitor the return of packages chanelled through our Calgary office. The questionnaire log contains respondent's demographic information and a status code. This code indicates whether the respondent is a newly identified outmigrant or someone who is already in the master list. This code also indicates whether or not the respondent is eligible.

These newly identified outmigrants reported by outmigrant respondents were usually members of the respondent's household who were reported in the enumeration form included in the standard package. If they had not yet been contacted, their names were listed in a log which monitored the mailing of new packages.

4.3.6.5 Follow-Up Strategies

While response rates on most mail surveys are notoriously low, (figures of 40-50 percent being the norm), it was the only method of data collection from potential respondents who were scattered all over the North American continent and as far as England, Australia, New Zealand, and the Caribbean Islands. Several strategies were used to maximize response rates:

a) Telephone Calls

From the ascertainment process, it was estimated that at least 70% of outmigrants were still residing within the Province of Alberta. In order to make telephone calls more efficient and economical as a means of follow-up, an office was set up in Calgary for this purpose. This office was in operation by the time of the first mailout. Attempts were made to contact every single individual in the outmigrant master list whose telephone number was available to us. The purpose of these calls was to encourage completion of the questionnaire and answer any questions they could have.

The covering letter in the mailout package also encouraged respondents to make collect calls to the project office if they needed further assistance in completing the questionnaires.

b) Second Mailout

The next step used to increase the response rate was mailing out a second package to those individuals who had not replied after the initial mailout.

4.3.7 Outstanding Issues

While a variety of tactics were used in order to maximize the level of accuracy in estimating the denominator for the outmigrant population, we make no claims at having obtained an exhaustive listing of the total outmigrant population in the

Index Area. However, these estimates provide the most complete denominator obtainable, given the major limiting factors of, i) the long period (28 years) explored, ii) the short period of time available for enumeration (three months), iii) the appreciable mobility of the target population, and iv) the special difficulties with addresses and frequent long-distance emigration of this rural population.

The effect of low response rates in this component is not clear. A possible indicator of the randomness of the responders will be assessed by comparing the resulting outmigrant groups on the basis of sociodemographic variables.

5. HEALTH STATUS EVALUATION

5.1 Crossectional Survey

5.1.1 Description

This component of the study consists of a crossectional epidemiological survey with three comparison groups.

5.1.2 Selection of Index Subjects

A complete census of all residents of the Index Area (IA) was taken and all persons enrolled belong to this group. Approximately one-third of these residents were evaluated in June, and the remainder in July 1985. The order of selection was arbitrary and at the convenience of participants, rather than random. This was to enhance attainment of high response rates.

5.1.3 Sampling of Unexposed Comparison Subjects

A geographical area of Southwest Alberta, demographically comparable to the Index Area, (see section 4.2) but not exposed to sour gas emissions, was found and provided the sampling frame for the main comparison group. This area was situated surrounding the towns of Stirling and Raymond, but did not include the town of Raymond. We call this area SR. The sample of individuals representative of this comparison area was selected in two stages.

Firstly, a complete census of all residents of the SR area was done by our enumerating team. A total of 1693 residents, living in 461 households, formed the sampling frame. The following were excluded: trailer parks because the residents were transients, Hutterite communities because their distinctly different living habits and small numbers made finding a suitable control impossible, and 25 households who could not be contacted. A tabulation of these residents by age and religion is given in Table 5.1/1

Secondly, in order to reduce the study group size (1693) to that required for a valid study (900), and to assure that at least one third of sample members were Mormons, a stratified probability random sample was drawn. See Table 5.1/2.

All 22 infants were excluded from the sample. Furthermore, no replacement sample was used because even all 22 would not provide useful information. A replacement sample of 63 was taken to substitute ineligibles and unreachable subjects following predetermined rules.

The sampling process was done using a computerized BASIC random number generating function, with varying sampling probabilities in order to reach the desired sample size while retaining known probabilities for each stratum.

TABLE 5.1/1

SAMPLING FRAME OF SR AREA BY RELIGION AND AGE

Age	Non-Mormon	Mormon	Total
15+	634	536	1170
5-14	142	231	373
1-5	33	95	128
<1	6	16	22
Total	815	878	1693

TABLE 5.1/2

SAMPLE OF SR AREA BY RELIGION AND AGE

Age	Non-Mormon	Mormon	Total
15+	350	200	550
5-14	142	80	222
1-5	33	95	128
<1	0	0	0
Total	525	375	900

5.1.4 Sampling of Exposed Representative Comparison Subjects

Another geographical area demographically representative of non-metropolitan Southern Albertans, but exposed to sour gas emissions was selected north of Calgary. This area, called DCCI, (abbreviation of Didsbury, Carstairs, Crossfield and Irricana), had few Mormon residents (less than 1%) and, therefore, was only comparable to Southern rural Alberta in general. Lifestyle differences such as alcohol and tobacco use may be important confounding variables in a health survey. Thus, for certain aspects of the study, it was considered best to be in a position to adjust for such confounding variables. The selection of the sample in this second comparison area was made in three stages: a census of all households, an enumeration of a random sample of households and a stratified random sample of individuals from the randomly selected households.

Firstly, a team established the listing of all households in the area, which we found to be 3652. Secondly, a random sample of 1000 households from these was selected. A complete enumeration was done in 856 of these. The remaining 144 had either died, moved away, had unlisted numbers or could not be reached during summer holidays. A total of 2219 residents were enumerated from these 856 households and their age distribution is given below:

	15+	5-14	1-5	<1
Frequency	1696	342	151	30

Thirdly, a stratified random sample of 495 individuals, was obtained. The age distribution is given below:

	15+	5-14	1-5	<1
Frequency	289	123	83	0

5.1.5 Data Gathering Procedures

Data for this study were obtained by means of an interviewer-administered questionnaire, a ritualistic medical examination, a laboratory profile, a judgemental medical examination and by prescriptive and discretionary use of tertiary medical consultation.

5.1.5.1 The Questionnaire

The categories of information elicited with the questionnaire are:

1) Demographic characteristics;

2) Risk factors;

3) Life style;

4) Self reported symptoms and illnesses;

5) Medical services utilization;

6) Disability;

7) Reproductive history.

The sections dealing with chronic illness, use of medical services and disability were identical to those used in the Canada Health Survey. Sections dealing with respiratory illness were identical with those used and validated by the American Thoracic Society 1978 Respiratory Symptoms Questionnaire. This was done to facilitate comparisons with other data sets.

Because some of the issues addressed in children were age-specific, three childhood questionnaires were prepared for ages 5 to 13 years, 1 to 5 years and 0 to 1 year. The latter was used only in the Index Area since the numbers of children in the 0 to 1 age category were too small in the control population to provide meaningful data. The questions about children were asked of one parent or guardian.

Each child questionnaire was linked to that of the parent for common demographic risk factor and lifestyle information.

5.1.5.2 The Ritualistic Medical Examination

The ritualistic medical examination was carried out by a physician specifically trained to carry out this type of examination. The physician examined the patient following a rigidly prescribed protocol and they recorded all findings without taking a history or enquiry about the person's health in any way. As indicated above, history of illnesses and symptoms was obtained independently to avoid biasing the examining physician's physical assessment. The adult examination protocol consisted of 74 specific items, many with several subsections. Because of age specific requirements, there were separate protocols for children and adolescents aged 0 to 1 year, 2 to 5 years, 6 to 9 years and 10 to 18 years.

Participants aged over 45 years were offered a rectal examination. A hemoccult test was part of this examination.

All females aged 18 to 60 years were offered a pelvic examination which included a Papanicolaou smear.

A university student trained by one of the co-principal investigators carried out a Denver Developmental Screening Test on all children aged 4 years, plus or minus 1 month.

5.1.5.3 Laboratory Data

Laboratory data include to physiological, biochemical, and toxicological measurements: height, weight, and visual acuity; electrocardiograms and spirograms; and serum for biochemistry and trace metal analysis of hair and blood. The methods for trace metal analyses and spirometry are discussed separately under Chapter 8; and the other measurements are discussed in this section.

Height and Weight: Height was measured in stocking feet with the breath held at total lung capacity. Very young children who could not stand up straight had length measured in the supine position. Weight was measured in stocking feet on a spring-loaded scale. Infants were weighed on a baby scale which used weights.

Visual Acuity: Eyes may be sensitive indicators to environmental pollution and eye damage can occur with exposure to high concentrations to sour gas. Visual acuity was measured for participants of at least 7 years of age using a standard 20 foot distance eye chart with letters (or symbols for those who were illiterate). Usual corrective lenses were worn during testing. Acuity was recorded for each eye as the lowest line of the chart above the line in which two or more errors were made.

Urine Analysis: Renal disease may be caused by exposure to certain heavy metals and urinalysis is commonly used in health screening. From participants at least 7 years of age, a midstream non-sterile urine sample was collected and analyzed by reagent strips (AMES multistix) for the following: specific gravity, pH, protein, glucose, ketones, bilirubin, blood, and urobilinogen.

Electrocardiography: Few environmental/occupational exposures have been associated with cardiovascular abnormalities (CS_2, CO, nitroglycerin). However, the health effects of chronic exposure to gas plant emissions are unknown and electrocardiograms were used to screen for possible cardiac abnormalities. A standard twelve lead electrocardiogram with computer interpretation (Marquette Mach II) was done by a trained technician for all participants at least 25 years of age. Gain was set at 25mm per second and 10mm per millivolt. The technician routinely used an internal 100Hz filter and the mechanisms to control baseline drift and muscle tremor. Electrocardiograms were performed. The technique was regularly verified by an internist. Age, sex, and race were entered for computer interpretation.

Reproducibility of the electrocardiogram interpretation over the duration of the study was tested as follows: from each testing day during July and August a simple random sample of one or two participants were retested during the last two weeks of August 1985. The results of reproducibility testing are presented in section 9.9. Other quality control measures are described in section 10.2.3.3

Biochemistry: Certain environmental/occupational exposures can cause renal or hepatic disease. In addition, the effects of chronic exposure to sour gas plant emissions are unknown. As another method of health screening serum was analyzed for total protein, albumin, calcium, phosphorus, cholesterol, uric acid, urea, total bilirubin, alkaline phosphatase, creatine kinase, lactate dehydrogenase, and aspartate aminotransferase. Serum was obtained from non-fasting participants at least 7 years of age. Approximately 7mls of blood were drawn by venipuncture of an antecubital vein following application of a proximal tourniquet. The blood sample was allowed to clot spontaneously (approximately

20 minutes at room temperature). A serum separator (Sure-Sep II^{R}, General Diagnostics) was placed in the tube which was then centrifuged for 10 minutes at 3500 rpm. Serum was poured into a plastic transport tube and refrigerated for a maximum of 4 days before being received by the Clinical Chemistry Laboratory of the Foothills Hospital (College of American Pathologists accreditation number CN001-003). Results from an automated analyzer (Technicon SMA II^{R}) were sent electronically, without transcription, to McGill University computer files.

5.1.5.4 The Judgemental Medical Examination

After the questionnaire, the ritualistic examination, and the laboratory sequence, participants went to the judgemental medical examination. This was carried out by a senior physician who had access to all the data gathered up to this point. He/she verified elements in the questionnaire, the ritualistic examination, and the laboratory data and then recorded his/her conclusions on a separate form. Whenever possible, a definitive diagnosis was established and recorded. In cases of doubt or when a participant specifically requested, tertiary specialist consultation was arranged at Foothills Hospital, University of Calgary, and the result was subsequently entered into the data set.

5.1.6 Outcome Variables

The outcome variables selected beforehand and the relevant data sources are as follows:

5.1.6.1 Current Physical Disability

Information was asked regarding bed disability, decrease in minor and major activities and, for children, school absence and reduction in usual play activity for the past two weeks.

5.1.6.2 Prevalence of Major Chronic Irreversible Illness

In the questionnaire, there were specific questions asking for the presence of predetermined health problems at the time of the interview. To facilitate the comparison with other data sets, we looked at the same problems and asked the same questions as the Canada Health Survey and a study done by the Principal Investigator in Toronto (Junction Triangle control labelled TC).

5.1.6.3 Clinical Findings

5.1.6.3.1 Cardinal Outcome Variables

Symptoms, signs, and diseases with plausible or known associations with exposure to environmental irritants were in sour gas emissions determined a priori to be the primary or cardinal clinical outcome variables. When hydrogen sulfide contacts moist tissues, an irritating alkaline sulfide is formed. Thus clinical findings related to external ocular, respiratory, and (to a lesser extent), cutaneous areas were considered to be of cardinal importance. Sub-acute exposure to hydrogen sulfide has been associated with a wide variety of neurological sequela such as headache, dizziness, and polyneuropathy. Also nausea and diarrhea suggestive of gastroenteritis has been reported. Thus gastrointestinal and neurological clinical findings were also considered to be of cardinal importance. Of all the clinical data gathered during the study, those related to cardinal clinical findings were given primary importance. Other clinical findings were assigned a lower priority.

Cardinal clinical findings include cardinal symptoms, signs, and diagnoses. The symptoms and signs are listed in the following two sections, and diagnoses in section 5.1.6.4.

5.1.6.3.2 Burden of Symptoms

In the questionnaire, 20 symptoms were asked for and information was obtained regarding the use of medical services and of medications. For 12 of them there was an enquiry regarding seasonality. Two-week and twelve-month prevalence was obtained. These symptoms were selected for their plausibility with regard to environmental exposure.

They include: 1° irritation symptoms (itchiness, burning, etc.) of nose, throat, eyes; 2° trembling, tingling, loss of feeling, weakness in extremities; 3° feeling of suffocation or shortness of breath when walking up a slight hill or upstairs; 4° tiredness or fatigue; 5° cough, wheezing or phlegm; 6° stomach discomfort.

5.1.6.3.3 Burden of Signs

The ritualistic medical examination provided information on 150 physical signs. Our analysis focused on a subset of 23 signs combined in a specific way to provide an index of environmental exposure.

Direct interaction of an environmental irritant with epithelial surfaces most likely resulted in diffuse, bilateral, manifestatious in exposed areas. These characteristics should apply either for primary irritants or allergens.

Accordingly, our analysis retained all the signs which alone or in combination would suggest damage to the eyes, nose, mouth and pharynx, lungs, and skin over the face and upper extremities.

Red eyes indicate evidence of irritation over lid margins or sclerae or conjunctivae. Red mucosa does similarly for nasal or buccal or pharyngeal mucosa. Neurological signs reflect loss of ankle reflexes, or weakness or loss of sensation (touch, or vibration or position) in feet. Tremor, wheezing and crackles in lungs, and ear drum abnormalities complete the list of cardinal signs we looked at. In an attempt to minimise bias, the examiners were not aware of this list of cardinal signs.

5.1.6.4 Prevalence of Disease

The prevalence of specific diseases/disorders were identified by a variety of methods:

a) Questionnaire: The prevalence of 23 non-malignant diseases/disorders and 8 malignant diseases were ascertained by questionnaire. We paid special attention to the most common problems and to the problems more plausibly related to environmental exposure.

b) Judgemental Medical Examination: Using information from the questionnaire, ritualistic examination, and available laboratory results, the judgemental physician made diagnoses where possible. To assist in making diagnoses, the judgemental physician was permitted to ask further specific questions and carry out further physical examination. In cases where the judgemental physician was unsure about the presence or nature of a disease, participants were referred to an appropriate medical specialist at the Foothills Hospital in Calgary, and any resulting diagnoses were included among the participants' data.

In addition to looking at the most common diagnoses made by judgemental physicians, we looked at the diagnoses plausibly related to environmental exposure. They include such things as: hay fever, asthma, chronic bronchitis, conjunctivitis, dermatitis, peripheral neuropathy, congenital anomalies, sinusitis, and emphysema.

c) Specific Conditions Defined by Formal Clinical Algorithms: Algorithms were created to measure the prevalence of certain specific conditions, many of which could be plausibly related to adverse environmental conditions. To establish content validity of these algorithms as indicators of syndromes/disorders, they were created in conjunction with medical specialists representing the fields of neurology, general internal medicine, respirology, pediatrics, and epidemiology. These algorithms were then applied to data elicited by the questionnaire, and/or ritualistic medical examination, and/or laboratory tests for each participant at least 15 years of age. (Algorithms were not applied to younger participants because the amount of data available was relatively less, on both the questionnaire and physical examination especially in the area of neurology. Moreover, those younger than 7 years old did not undergo many of the laboratory investigations that were previously described.) The advantage of this approach to ascertain prevalences of specific conditions was that the algorithms themselves were completely reproducible and were applied identically to all participants in all areas.

5.1.6.5 Utilization of Health Services

a) The questionnaire: Questions were asked of participants regarding the use of physicians, hospitals, and medications for a wide variety of symptoms and diagnoses.

5.1.6.6 Mortality

To check for bias, either while answering a questionnaire or through telephone contacts, participants were asked to give the names of people (family or friends) they knew who had lived in the area and died since 1957. Mortality rates were calculated from vital statistics sources for the contrasts related to the hypotheses of this study.

5.1.7 Duration of Exposure

The duration of exposure to gas plant emissions was measured by asking participants how long they have lived in the area.

5.1.8 Potential Confounding Variables

The following potential confounding variables have been taken into account:

a) Demographic variables: Age, sex, marital status, occupation, education, religion, socio-economic status;

b) Lifestyle factors: Use of alcohol and tobacco; diet. Religion as a proxy for lifestyle was also used as a co-variate;

c) Family history of inherited disease;

d) Environmental factors: Type of housing, heating, insulation; water supply; source of food; exposure to dust, noise, chemicals, solvents, fumes, herbicides and insecticides.

5.1.9 Contrasts of the Study

The main purpose of the study was to determine whether there was an "epidemic" of adverse health experience among residents of the Index Area. To that end, the main contrast for the crossectional survey of the study is to determine whether an epidemic has affected Index Area residents. That contrast declared *a priori*, is the principal one for statistical considerations between the Index Area (IA) and the Stirling/Raymond area (SR). (See Figure 5.1/1).

A first ancillary contrast is between IA and the exposed representative control area in Didsbury, Carstairs, Crossfield and Irricana (DCCI). Should there be differences between IA and SR, most particularly should IA be in worse health than SR according to our indicators, the comparison with DCCI which is also exposed should give the first clues about the likelihood that sour gas emissions are responsible for such adverse effects. If the residents of the DCCI area have adverse health profiles compared to SR, and similar to the IA profiles, the evidence starts to be much more solid than it would have been with only one comparison.

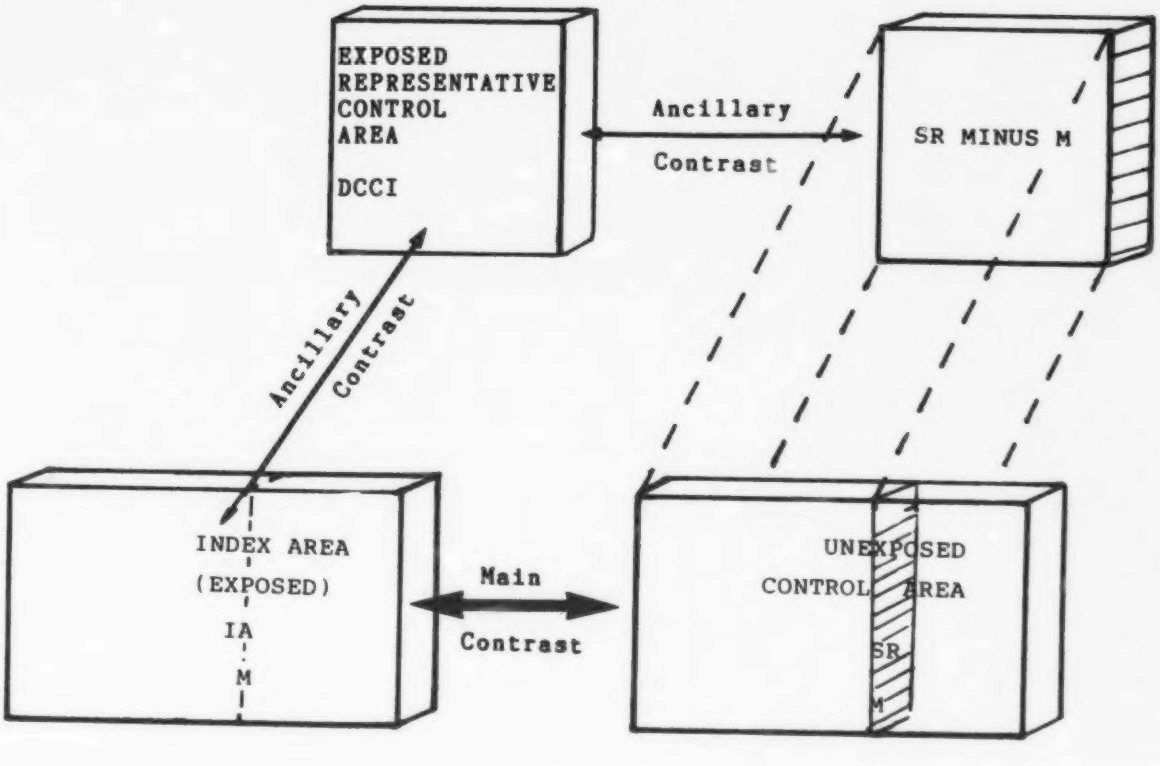
By removing Mormons from the SR sample, we are left with what we called the SR minus M group. We have established that this group is not only very comparable to the DCCI, but both are very comparable to Southern non-metropolitan Albertans in general. Thus, a second ancillary comparison, DCCI contrasted to SR minus M, would further buttress the validity of any findings in the main contrast, particularly if they are of the same direction and of the same order of magnitude.

Moreover, although the interpretation would have to be guarded and cautious, the contrast of DCCI with SR minus M would shed some light on the possible effects of sour gas emissions on representative non-metropolitan Albertans since, we insist, both populations are highly similar to each other and each in turn to the entire rural population of Southern Alberta.

Should all contrasts, the main contrast and the two ancillary contrasts show no statistical and clinical differences in any direction, this would be very strong evidence suggesting that there no adverse health effects to the residents of the Index Area and to the representative area of rural Albertans in general are demonstrable.

FIGURE 5.1/1

PLANNED CONTRAST FOR CROSSECTIONAL SURVEY


EXPOSED
REPRESENTATIVE
CONTROL
AREA
DCCI
Ancillary
Contrast
SR MINUS M
Ancillary
Contrast
INDEX AREA
(EXPOSED)
IA
M
Main
Contrast
UNEXPOSED
CONTROL AREA
SR
M

M = Population of Mormon religion

FIGURE 5.1/1 (continued)

PLANNED CONTRAST FOR CROSSECTIONAL SURVEY

Note: IA and SR are very similar sociodemographically. DCCI and SR-M (Mormons excluded) are very comparable sociodemographically. DCCI very similar to all 119 provincial census tracts south of Edmonton (considered together) excluding Edmonton and Calgary.

Main Contrast: IA compared to SR

- to establish whether there is an "epidemic" of compromised health among residents of the Index Area IA;
- settles main questions of study as set forth in advance.

Ancillary Contrast:

IA compared to DCCI

- in the event of differences found between IA and SR, verifies whether there are consistent patterns of change that could point to exposure as a plausible candidate for causal significance.

DCCI compared to SR-M

- in the event of differences found between IA and SR, if the same direction and magnitude is observed between DCCI and SR-M then the validity of findings for the main contrast (IA vs. SR) is buttressed;
- the contrast of DCCI vs. SR-M sheds some light on the possible effect of sour gas emmissions on representative non-metropolitan Albertans since both populations are highly similar to each other and each in turn to the entire rural population of southern Alberta.

5.1.10 Feed-Back to Participants

Participants received personal feed-back on their medical diagnostic review findings at the time of meeting the judgemental physician for all items except biochemical tests and heavy metal determinations. Those individuals sent to Calgary for tertiary consultation received feed-back either from the consultant directly, from the study team, from their personal doctor, or from all of these.

Biochemical and heavy metal test abnormalities were communicated directly to participants by telephone or by mail as soon as they become available and appropriate action was suggested. Details of the follow-up mechanisms used are found in Appendix 14.1.

If abnormalities were found the participant was informed free of charge. For those participants who had normal findings, results are available upon submission of a witness letter of request and payment of a fee.

5.2 Cohort Analytic Historical Follow-Up

5.2.1 Description

As discussed in section 4.1, a longitudinal follow-up of persons in the different areas was important to eliminate the possible contribution of any differential health-related selective migration. A crossectional study alone cannot identify this type of bias or eliminate concern about such a phenomenon.

Aside from all the outcomes related to the cancer and reproductive studies, other important outcomes like diagnoses of serious diseases could be compared among the three study areas, using the longitudinal or cohort design. This approach permits a check on the health status evaluation, to detectable bias due to health-related selective migration.

5.2.2 Creation of Cohorts for Health Status Evaluation

The cohort study of these key outcomes is possible because the occurrence of these same outcomes was measured comparably in all outmigrants as explained in section 4.3.

Because only samples were studied in the control areas, the enumeration of the outmigrants had to be limited to close relatives of the participants. This was the only feasible approach to generating a subset of outmigrants similar to the larger group identified in the Index Area.

Consequently, the cohorts compared for the health status evaluation were formed in the following way:

1) Index Cohort: This cohort includes all the participants seen in the summer 1985 and who were also living in the area in 1970. Added to this group are the outmigrants identified by the 1985 participants as close relatives and as living in the area in 1970, as well as those residents of the area who had died since 1970. The choice of 1970 is explained in section 4.1.

2) Control Areas Cohorts: These cohorts include all the participants in each area, seen in the summer 1985 and who were also living in their respective areas in 1970. Added to these are the respective groups of outmigrants identified by the 1985 participants as close relatives and living in the area in 1970, as well as those residents of the area who have died since 1970.

The three cohorts are then similar because they were formed in a comparable way. But they are not necessarily representative of the true cohorts who lived in the respective areas in 1970, because the group of outmigrants is relatively underrepresented in our cohorts. We posit, however, that the rates generated in the cohort study are similar. Theoretically, if they are affected by systematic error then the direction and magnitude of the bias should be the same. An indication of the similarity of these cohorts will be suggested by the comparison of the main demographic variables.

5.2.3 Types of Data Collected

In addition to the basic information on gender, date of entry and exit in the area, date of birth, cancer, reproductive outcomes, the questionnaire asked about the time of onset and the occurrence of the following diseases: heart disease, hypertension (high blood pressure), migraine headaches, epilepsy, arthritis, chronic bronchitis or phlegm lasting more than a year, emphysema, and diabetes.

The date and cause of death were available in the outmigrant lists described in section 4.3

5.3 Statistical Analytic Methods

In this section, the statistical aspects of the study are described.

5.3.1 Measures of Effect

In the case of continuous outcome measures such as the number of days of activity loss, mean difference (MD) was used to assess the effect of exposure. For dichotomous variables both differences of proportions (PD) and ratios of proportions (PR) were used to measure the exposure-outcome relation.

5.3.2 Clinical and Statistical Significance

Because of the large sample size of this study, the sole use of statistical significance as a criterion of importance of the effects observed would be incorrect. The clinical significance of a result is also invoked to assess the meaning of differences. As declared in advance in the protocol, proportion differences of the order of 10% to 20% are deemed clinically significant. We chose a difference of 20% for frequent outcomes and 10% for less frequent outcomes. Infrequent outcomes were defined as those with a proportion less than 10% in the unexposed control area. These differences correspond to proportion ratios of the order of around 1.5 to 3.

5.3.3 Effect of Sample Size

The effect of sample size on the level of statistical significance was computed conservatively for dichotomous data only. The computations are also based on two age groups (less than 15, 15 or more) and in terms of unadjusted analyses. The effect of the sample sizes is assessed using the power of the test, i.e. the chance of finding a true given effect, for a fixed significance level of 1%, i.e. the chance of finding an effect erroneously. We opted for a power large enough (at least 90%) to reduce the risk of not finding true effects, as well as a significance level low enough (1%) to reduce the risk of declaring unimportant effects significant. Based on these criteria, sample sizes of 600 (300 adults, 300 children) in each control area were deemed sufficient. The adjustment to the protocol (July 1985) increased the sample size requirement of the SR area from 600 to 900.

5.3.4 Potential Confounding Variables

Although attempts were made to attain a high level of similarity between the groups of comparison, we expected that certain demographic and lifestyle factors could differ among the groups. Such factors might also be related to the outcome variables under study. Such factors, referred to as confounding variables, were first investigated individually and then simultaneously in terms of their effect on the result for each key outcome variable and contrast. The list of the factors considered to be potentially confounding includes all sociodemographic characteristics (age, religion, education, etc.), lifestyle habits (smoking, alcohol consumption, etc.), occupation, professional exposures, and others. The length of residence in the area has also been used for adjustment.

5.3.5 Quantification of Key Outcome Variables

Although most key outcome variables described in section 5.1.6 are clearly defined and do not require any quantification process, some are more elaborate and do require the description of this process. For instance, the prevalence of chronic irreversible illness, the incidence and prevalence of definite diagnoses, mortality, and the utilization of health services do not require any elaboration as individuals with a given condition are counted and proportions calculated.

For current physical disability in the last two weeks, individuals with some activity loss (frequency), are reported by the proportion of days free of any activity loss and the average number of days of activity loss.

For the burden of symptoms in the two weeks and the 12 months preceding the interview, in addition to the prevalence of each of the 15 symptoms probed, which include the 5 cardinal symptoms, the proportion of individuals with at least one (cardinal) symptom and the mean number of (cardinal) symptoms will be used to assess this burden.

For the burden of physical signs detected during the ritualistic examination, in addition to prevalence of certain specific signs of interest (cardinal signs), the distribution of the number of signs was used to assess this burden in order to be able to evaluate the global frequency.

5.3.6 Statistical Techniques

Classical methods of statistical analysis were used to assess the effect of exposure. In a first instance, univariate techniques, such as chi-square and student's t tests, were used to compare the distributions of the key outcome variables.

More formal comparisons of the groups and estimations of the measures of effect were performed using multiple regression methods in order to eliminate the effect of any potential confounding variables. By using a stepwise, but not automatic, approach, we were able to eliminate these potential confounding variables when they had no effect on the analysis. The resulting measures of effect are therefore adjusted for the factors which truly confound the contrast. When no factors were found to be confounding, only the crude measures of effect are presented for simplicity's sake.

In view of the reasons given in section 11.2, the resulting significance levels were only rarely reported.

6. STUDY OF CANCER RISKS AND OUTCOMES AS A COMPONENT OF THE MDR

6.1 Study Design of the Cancer Component

6.1.1 Description

6.1.1.1 Orientation

The cancer component of the study was undertaken because of the perception on the part of the residents of the Index Area that the occurrence of cancer among residents of this area has been higher than they expected. No particular site for cancer has been singled out as being of special concern, and the residents appear to be alarmed by a perceived unusual overall cancer experience. These concerns have arisen during the years since the first local sour gas refinery began functioning in 1957. Therefore, when the Southwest Alberta Medical Diagnostic Review Project (MDR) was commissioned, there was a clear mandate to incorporate a definitive assessment of the occurrence of cancer among residents of the Index Area. The purpose of this component of the MDR is to study the cancer experience of residents of the Index Area and to determine whether this experience is other than that which would be expected based on reference populations. It is not an objective of this study to demonstrate an etiologic association between exposure to sour gas emissions and cancer. Rather, the specific a priori objective of this part of the study is to test the hypothesis that the incidence of cancer among Index Area residents has been higher than that which should be anticipated in such a population.

6.1.1.2 Background

Several studies have examined the atmospheric pollution caused by sour gas plants in the Index Area, and some of these have dealt with health effects. Of particular pertinence to the question of cancer are two documents prepared by the Alberta Department of Social Services and Community Health. The first document, titled "Comparative Analysis of Health Statistics for Southwest Alberta Communities", was published in April 1983. This report examines general mortality, perinatal mortality, cancer incidence, the incidence of congenital abnormalities, and sudden infant deaths occurring over a varying number of years in Twin Butte and eleven other communities in Southern Alberta, namely: Bow Island, Mill River, Raymond, Taber, Cardston, Magrath, Forth MacLeod, Claresholm, Vulcan, High River, and Turner Valley. It also presents crude cancer incidence rates [excluding non-melanotic cancer of the skin and carcinoma in situ of the cervix (CIS)] for Municipal District 9 (which includes the town of Pincher Creek and about 60% of the Index Area), for Census Division 3 (which contains all of the Index Area), and for the entire province of Alberta for the years 1961-81. Site-specific cancer incidence rates for Census Division 3, standardized by age to the 1971 Alberta census population, were derived for the years 1961-81. No major increases or decreases in cancer for the areas including the Index Area were encountered in this analysis other than a small elevation in the incidence of non-melanotic cancer of the skin, which is generally found to be higher in Southern Alberta and thought to be related to increased exposure to sunlight in this area (Cancer Registration in Alberta, Provincial Cancer Hospitals Board). Enumeration of cancers in Municipal District 9 for the years 1966-80 failed to demonstrate any unusual incidence of cancer in either men or women.

In December 1984, a document titled "Comparative Analysis of Hospital and Physician Utilization Practices in Southwest Alberta Communities" was published by the Health Services Division of Alberta Social Services and Community Health. The analysis in this latter report was based on separation statistics and patient-day statistics for hospitalizations occurring during the period 1975-77. In addition, physician-visit statistics for 1977-79 were obtained from Alberta Hospitals and Medical Care. Data from twelve general hospital districts in Southwestern Alberta (including Twin Butte) were utilized. Separation statistics were gathered according to the 6 following grouped causes of hospitalization: neoplasms, upper respiratory infections and influenza, pneumonia, asthma and bronchitis, spontaneous abortion, and congenital anomalies. Age-standardized rates for each sex were compared across the twelve communities. The results showed that according to the available sources, residents of the general hospital district of Twin Butte were no more likely to be hospitalized or to visit a physician than residents of neighboring communities for any of the causes examined. With regard to separation rates for neoplasms in particular, Twin Butte males ranked last while Twin Butte females ranked sixth among the twelve areas studied.

6.1.2 Objectives

The major objective of this component of the MDR was to determine whether the incidence of cancer (as registered by the Alberta Cancer Registry) during the period January 1, 1970 to December 31, 1984 among all individuals who were alive and resident in the Index Area at anytime in 1970 was higher than that which should be expected in socio-demographically similar populations in Southern Alberta during the same period.

Secondly, because of significant local concerns with respect to differences in the cancer experience among the various communities comprising the Index Area (i.e., Mountain View, Hill Spring, Glenwood, Willow Creek, and the Pincher Creek region which includes Twin Butte), the community specific cancer point prevalence for the Index Area health survey participants (93% of the enumerated Index Area population participated) was to be compared.

6.1.2.1 Definitions

For ease of communication, we will make some definitions which will apply henceforth throughout this document. These are elaborated in section 4 above but are included here to clarify the Cancer Study design description.

Index Area = An area of Southwestern Alberta in and around the towns of Twin Butte, Glenwood, Hill Spring, Willow Creek and Mountain View. This area delineated by officials from Alberta Environment. The geographic boundaries used by the Southwest Alberta Medical Diagnostic Review Project are shown in Figure 1/1.

Index Area 1970 cohort = The collection of all individuals who were alive and resident in the Index Area during the calendar year 1970.

Incidence Period = January 1, 1970 - December 31, 1984

Supplemental Incidence Period = January 1, 1985 - December 31, 1985

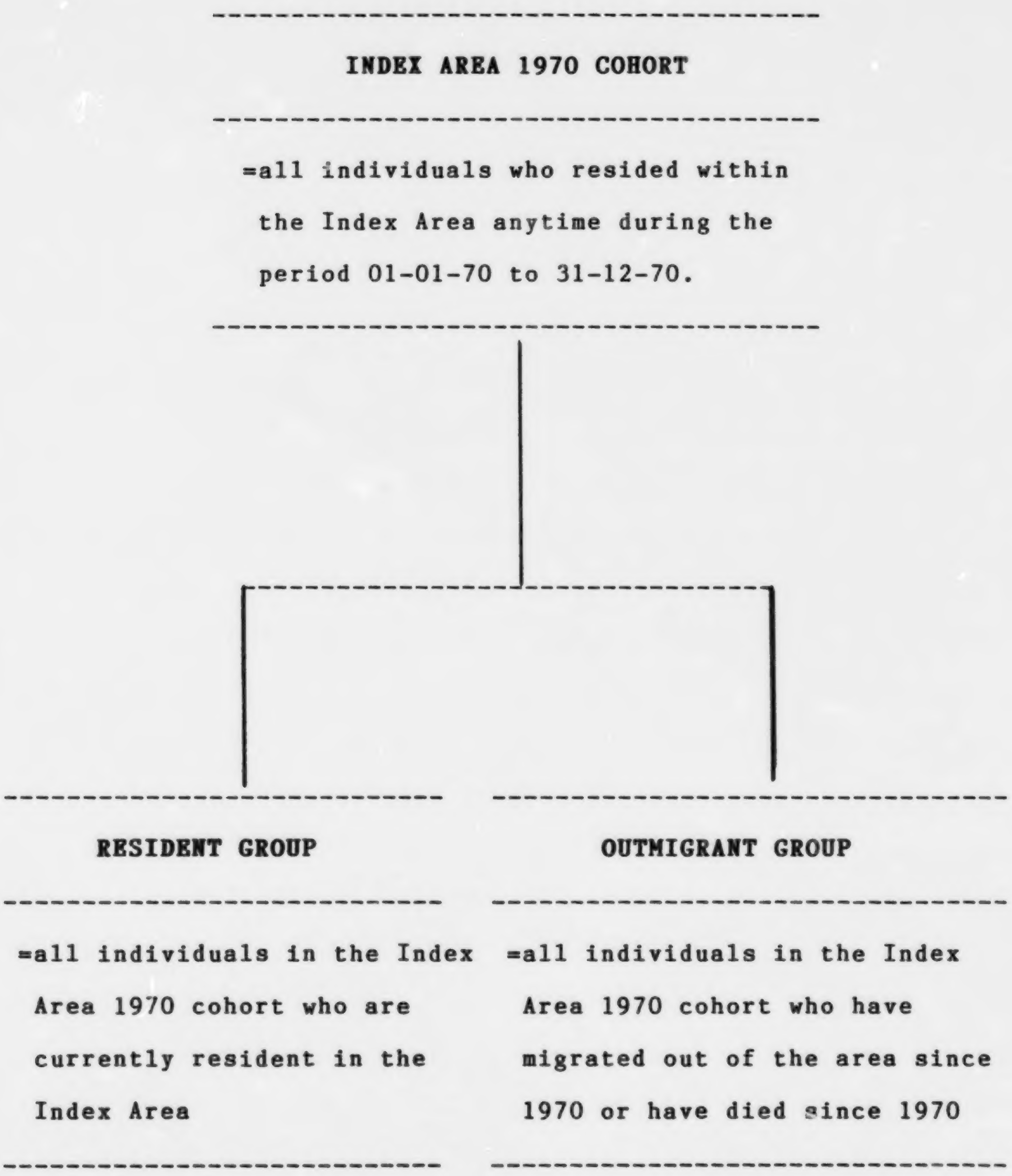
Incident Cancer = Any cancer occurring in a member of the Index Area 1970 cohort during the incidence period as registered by the Alberta Cancer Registry. Under this definition, only cancers that occurred within the Province of Alberta will be registered and thus be considered as incident cancers.

Standardized Incidence Ratio (SIR) = The ratio of the observed number of incident cancers divided by the number of expected cancers, where the latter is obtained by applying age-, sex-, and cohort-specific incidence rates derived from referent populations to the IA 1970 cohort.

6.1.3 Cohort Definition and Enumeration

This cohort was defined to include anyone who resided in the Index Area any time between January 1, 1970 and December 31, 1970 (Figure 6.1/1). It was decided *a priori* that this cohort and its subsequent cancer experience would form the basis for the hypothesis test concerning the cancer experience of the Index Area. The choice of this cohort was acknowledged at the outset as having a number of strengths and limitations. First, the 1970 residency requirement excludes two groups of people who were theoretically at risk of developing cancer during the incidence period, namely children born in the area since 1970 and individuals who had migrated into the area since that year. Exclusion of these two groups was deemed acceptable since cancers that arose within these two populations would in most cases not have had plausible latency periods. Second, the 1970 residency requirement excludes individuals who left the area prior to 1970 or who died prior to 1970. However, there were concerns about the accuracy of information that could be obtained about these early residents. Moreover, the reliability of cancer registry records pertaining to the years 1957-69 is less than those pertaining to the more recent past. Many of these residents who left in the early years just after construction of the refineries may not have had reasonable durations of exposure nor could accurate information about their exposure and period of residence in the area be guaranteed. It is conceivable that recall about

Figure 6.1/1



INDEX AREA 1970 COHORT

=all individuals who resided within the Index Area anytime during the period 01-01-70 to 31-12-70.

RESIDENT GROUP

=all individuals in the Index Area 1970 cohort who are currently resident in the Index Area

OUTMIGRANT GROUP

=all individuals in the Index Area 1970 cohort who have migrated out of the area since 1970 or have died since 1970 early residents could be enhanced for those suffering an unusual event such as death from cancer so that recall of early residents might be biased. In summary, use of the Index Area 1970 cohort was felt to yield the optimal combination of reasonable exposure durations, plausible latency periods, sufficient subsequent observation time, increased accuracy of recall concerning outmigrants together with maximal availability, and reliability of local and provincial registry information.

The incidence period of 1970-84 offers several similar advantages. First, cancers that occurred within this time interval can reasonably be assumed to have had a plausible latency after first exposure to sour gas. Second, as mentioned above, although records of the Alberta Cancer Registry go back the 1950's, we were informed by Registry officials that early records are of limited reliability and capture, while those pertaining to the incidence period are of greater quality. Third, the incidence period chosen encompasses exactly three five-year periods (1970-74, 1975-79, 1980-84) and national census information is available for each period (1971, 1976, 1981). This facilitated the calculation of expected rates in comparison populations.

The formal Incidence Period does not include cancers diagnosed in 1985. We were informed by Alberta Cancer Registry officials that there is often a considerable lag time before confirmed cancers are recorded by the registry. Thus, registry information for 1985 was incomplete, at the time of this study and we decide, to terminate the incidence period at the end of 1984. However, for completeness, we undertook a separate investigation of cancers diagnosed in 1985 (denoted the Supplemental Incidence Period). This was done to check whether there has been any unusual trends in cancer incidence during the very recent past. During the summer of 1985, 93% of Index Area residents underwent a full multiphasic health examination with subsequent secondary and tertiary referral. This was anticipated to lead to the early diagnosis of some cancers and was expected *a priori* to have the potential to artifactually inflate the cancer incidence in the Index Area during 1985. Because of the delay in registry recording and the possibility of *diagnostic surveillance bias*, the year 1985 could not be included in the formal Incidence Period, and the period was investigated separately.

It is convenient to define two subgroups of the Index Area 1970 cohort as depicted in Figure 6.1/1. The first subgroup, denoted the Resident Group (RG), is defined to consist of all members of the Index Area 1970 cohort who are currently resident in the Index Area. The second subgroup, denoted the Outmigrant Group (OG) is defined to consist of the remainder of the Index Area 1970 cohort, and includes all individuals who migrated out of the area since 1970 as well as all those who have died since 1970. These latter individuals are not strictly outmigrants, but the term Outmigrant Group is retained for simplicity. Enumeration of the RG and the OG were carried out separately, and methods for their enumeration are discussed in the following sections.

6.1.3.1 Enumeration of the Resident Group

Methods for the enumeration of the Index Area in preparation for the comparative health survey have already been discussed. This enumeration was carried out during the period June-July 1985. At the time that an Index Area resident visited the study site, an extensive questionnaire which included a detailed residential history was administered. Thus, for each current resident of the Index Area, it was possible to determine whether that resident was a member of the Index Area 1970 cohort. Such individuals constituted the RG. Only individuals who participated in the health survey were eligible for inclusion in the RG. Since the participation rate was approximately 93% among enumerated individuals, there were approximately 7% of residents of the Index Area (not all of whom would have been alive or living in the area in 1970) who did not participate in the health survey and, therefore could not be considered eligible for inclusion in the RG.

6.1.3.2 Enumeration of the Outmigrant Group

The enumeration process of the outmigrants relevant for this component of the study is described in section 4.3.4.1 for the Index Area.

In addition to the steps described there, further editing was done in the light of the objectives of this component. The vast majority of identified outmigrants was replicated from several sources, and the information from these sources was combined into a single record in such a way as to enhance overall accuracy. In addition, a certainty code was assigned to each outmigrant to indicate the overall quality of information as follows: where there were no discrepancies, all information concerning the outmigrant was combined into a single record and a certainty code of 1 was assigned; where there were discrepancies involving dates but where these were less than 5 years in duration and did not affect person-years of risk, a certainty code of 2 was assigned; finally, when discrepancies of greater than 5 years were present or where there were differences which would affect the total person-years of risk calculation, a certainty code of 3 was assigned. For any individual for whom a mailed outmigrant questionnaire was subsequently completed and returned, the information was updated appropriately and a certainty code of 1 was assigned.

To illustrate this, suppose 2 reports stated that the same outmigrant moved from the Index Area to another part of Alberta in 1973 and 1977 respectively. In such a case, a certainty code of 2 would be assigned since the discrepancy is under 5 years and since person-years of life within Alberta is the same in either instance. In cases of larger discrepancies, discretionary choices had to be made in order to maximize the quality of information. All decisions made in the final editing of the outmigrant file and all assignments of certainty codes were made without any knowledge of subsequent events such as cancer in these individuals. Hence, these decisions should not introduce any bias. Second, we adopted a priori the policy that when there were incongruous sets of data of equal quality, the one which gave rise to a lower total person-years of risk would be chosen. Thus, if any error was introduced, it was liberal in the sense that person-years of risk and hence number of expected cancers would be lowered, and hence standardized incidence ratios would be elevated. The establishment of the certainty code was done so that analyses could be stratified by certainty to check if any systematic error had been introduced.

Upon completion of this process, the Outmigrant Group (OG) was defined to consist of all individuals in the outmigrant file with accurate birth date information whose year of entry into the Index Area was before or during 1970 and whose year of exit from the Index Area (via migration or death) was during or after 1970.

This latter criterion was used to establish residency in 1970 and therefore membership in the Index Area 1970 Cohort.

6.1.4 Enumeration of Incident Cancers

Several sources were utilized in the enumeration of incident cancers. First, the investigators were given a confidential document entitled "Pincher Creek Municipal District Informant List of Serious Illnesses" which contained the names of 45 individuals from this general area who were reported to have developed cancer. We believe that this list was compiled by concerned individuals in the area in order to document what was believed to be an unusual cancer experience. However, a specific cancer site was given for only 18 of these individuals and no dates of diagnosis were given for any of the 45 people listed. Second, at the time of the Index Area health survey visit, every individual in the Index Area was asked to provide a list of friends or relatives from the Index Area who had developed cancer anytime since 1957. For each such individual, the respondent was asked to supply the full name, type of cancer, date of diagnosis, and date of death if applicable. For convenience, the information obtained from this process will be referred to as the "Health Survey Cancer Reports".

These two lists served only as adjunct sources of information. For the definitive identification of an incident cancer, we relied on our third and most important source of cancer information, the Alberta Cancer Registry. The process of enumerating incident cancers among the Index Area 1970 cohort was as follows:

Step 1

First, separate computerized listings of the Resident Group and the Outmigrant Group were prepared. These files included surname, first name, middle name, maiden name if applicable, date of birth, date of death if applicable, and self-reported history of cancer if any. These files were stored on magnetic tape and sent to officials of the Alberta Cancer Registry in Edmonton.

Step 2

A computerized record linkage with the files of the Alberta Cancer Registry was performed separately for the Resident Group and for the Outmigrant Group. This process involves converting surnames to Soundex equivalents and then searching for Soundex and sex matches between the files. For each such match identified, birth dates are then compared and those for whom birth dates match exactly or differ by less than five years are identified. This process is highly sensitive but only moderately specific to the presence of matches. In addition, a second computerized linkage based on maiden name was performed. To identify the true matches, two further manual searches were conducted. In each instance, the entire Resident Group and the entire Outmigrant Group were checked against all potential matches with respect to exact spelling of names, exact birthdates, current address, and date of death if applicable. It was during the manual checks of the linkage information that the use of the adjunct sources of cancer information, namely the Informant List and the Health Survey Cancer Reports, were used. Specifically, in the case of questionable links, reference was made to these lists in order to establish the accuracy of the link. Links involving ICD-9 codes between 140.0 and 208.9 were scrutinized most carefully as these involve malignant conditions. In many instances these reported links involved benign conditions; these were ignored since their inclusion or exclusion would not affect the estimates of the incidence of malignant disease. In a separate process, all self-reported cancers were linked manually to the Alberta Cancer Registry in order to confirm each reported case.

6.1.5 Reference Populations

Referent Population 1 (RP 1) = All Southern Alberta excluding the metropolitan areas of Calgary, Lethbridge, and Medicine Hat.

Referent Population 2 (RP 2) = Census Division 6 excluding Calgary.

Referent Population 3 (RP 3) = Census Division 2 excluding Lethbridge.

ICD - 9 = International Classification of Diseases, ninth revision

6.2 Statistical Analysis of the Cancer Component

6.2.1 Standardized Incidence Ratios

Incident cancers, defined to be those occurring in the Index Area 1970 cohort and diagnosed anywhere within Alberta during the years 1970-1984, were enumerated via linkage with the Alberta Cancer Registry as described above. Expected rates were derived for the three socio-demographically similar referent populations. The null hypothesis was that when standardized incidence ratios (SIR) were generated based on age, sex and five-year specific person-years of risk utilizing rates derived from the referent populations, the SIR's would be equal to 1.0. The significance of the SIR's was tested by computing 95% confidence intervals around them using methods described by Ederer and Mantel (1974) for calculating confidence limits on the ratio of two Poisson variables.

To obtain the standardized incidence ratios, it was first necessary to calculate the person-years of risk experienced by the Index Area 1970 cohort during the 1970-84 incidence period. Person-years of risk were classified by age group, sex, and 5-year time interval, that is, 1970-74, 1975-79, 1980-84. The age grouping was that in routine use at the Alberta Cancer Registry and was specified prior to the analysis. Since the outcome event in this study is an incident cancer registered by the Alberta

Registry, to be "at risk" for such an event, an individual must be alive and resident within Alberta. Thus, person-years of life within Alberta during the incidence period is the parameter to be measured and these were calculated in the conventional manner for each age group, sex, and five-year interval. For example, a 50 year old man alive in 1970 who survived the entire Incidence Period and who remained in Alberta contributed 5 person-years of risk to the 45-54 year old male age group during the period 1970-74, 5 person-years of risk to the 55-64 year old male age group during 1975-79, and 5 person-years of risk to the 55-64 year old male age group during the period 1980-84. For those leaving the at-risk group via migration out of Alberta or via death, the number of person-years of risk was calculated by conventional methods. Namely, for the final year of residence in the Index Area, one half year of risk was assessed. Similarly, for those few individuals in the Index Area 1970 cohort who entered the area in 1970 or were born in 1970, one half year of risk for their initial year of residence was assessed.

To complete the calculation of expected numbers of cancers, age-, sex-, and time-interval specific incidence rates were derived for the 3 referent populations and applied to the person-years of risk experienced by the Index Area 1970 cohort. The first of these referent populations was the Southern Alberta non-metropolitan population which was chosen because it more accurately reflects the nature of the Index Area cohort than would the traditional general Alberta incidence rates, which would include large metropolitan areas and thus potentially bias the results. The second referent population, i.e., 1981 Census Division No. 6 excluding Calgary, was chosen because it contains within its boundaries the entire referent area of DCCI (Didsbury-Carstairs-Crossfield-Irricana) utilized in the comparative health survey. The third referent population was the 1981 Census Division No. 2 excluding Lethbridge, which includes the entire second referent area for the comparative health survey, described as Stirling/Raymond. The data required for the referent population analysis were kindly provided by the Alberta Cancer Registry.

6.2.2 Effect of Sample Size

Sample size calculations were carried out prior to the study and were based on a prior estimate of 2000 people in the Index Area 1970 cohort with an incidence period spanning 15 years. This yields 30,000 person-years of observation. The 1978 crude all cancer incidence rate based on general Alberta population data is 3.4 cancers per 1000 person-years of observation. (Cancer Registration in Alberta, 1978, Alberta Cancer Board). Based on this, approximately 102 incident cancers would be expected if referent population rates hold; this would yield greater than 90% power to detect elevations in relative risk on the order of 1.2 for all cancers combined and 1.5 for major focus of cancer. By using a one-sided test with alpha = 0.05, the power to detect risks as small as 1.25 is approximately 70%. If non-melanotic skin cancer and cervical carcinoma in situ are ignored, the 1978 Alberta crude incidence rate is roughly 2.5 per 1000 person-years (which would yield about 75 incident cancers with 30,000 person-years of observation).

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Ederer F, Mantel N. Confidence limits of the ratio of two poisson variables. American Journal of Epidemiology 1974;100:165-167.

7. STUDY OF REPRODUCTIVE RISKS AND OUTCOMES

7.1 Study Design

7.1.1 Description

As described in section 2.1, the general objective of this portion of the project was to determine whether the frequency of reproductive abnormalities and birth defects in a population exposed to sour gas emissions differs from that observed in a demographically similar population elsewhere that was not so exposed. More specifically, the original aim stated in the McGill proposal to the Alberta Acid Deposition Research Program, was to develop a scientifically valid method for determining whether residents in an exposed (Index) area are at increased risk for adverse reproductive outcomes, or for inadequate development during childhood.

Four major goals were originally stated as follows:

1) Identification of community perceptions of the possible relationship between "sour gas" and adverse reproductive outcomes.

2) Collection of objective data on reproductive outcomes, with clinical validation where possible.

3) Comparison of objective measures of adverse reproductive outcomes from the Index Area with similar measures from appropriate comparison populations.

4) Determination of the feasibility of mounting a comprehensive epidemiological study that could yield an unequivocal test of the null hypothesis that exposure to sour gas in the Index Area is not associated with adverse reproductive outcome, or with inadequate development during early childhood. Whether such a study would be recommended was to depend on whether there were any indication of adverse outcomes from the comparisons in 3) above, as well as feasibility.

In summary, the major approach to this part of the study was: 1) the administration of a specially designed questionnaire to women on their reproductive outcomes, as a supplement to the general health status questionnaire, and 2) question inclusion in the medical histories and physical examinations of elements designed to identify the major and some minor birth defects, and major problems in the development of young children.

Three reproductive outcomes were examined that might be adversely affected by exposure to a noxious agent primarily during pregnancy. These were:

1) Fetal loss;

2) Prematurity and low birth weight;

3) Birth defects.

These will be discussed as "short term exposure" effects.

Two others were studied for which the exposure might be cumulative during the whole period of an individual's exposure. These were:

4) Infertility;

5) Inadequate childhood development.

These will be discussed as "long term exposure" effects.

The reproductive histories supplemented by data from other sources, provided retrospective data on the 1985 cohort of women for the outcomes of all their previous pregnancies. It also indicated whether the pregnancy was conceived and carried in an "exposed" or "unexposed" area, because the dates of residence of each woman in the areas studied were also recorded and the dates when the gas plants were operating are known.

The medical examination data for children expanded the data base and provided for validation of some of the outcomes reported by the mothers in a sample of subjects.

Short Term Exposure Effects

The major part of the study analysis of the "short term exposure" outcomes consisted of comparisons of incidence rates of adverse outcomes of pregnancy during which time members of the 1985 cohort were "exposed" or "not exposed", in the Index and comparison areas, for the years after the sour gas emissions began (Circa 1957). Similar data on outmigrants were examined to ascertain whether selective out-migration individuals could have affected comparisons of reproductive outcomes between the study populations.

Long Term Exposure Effects

The reproductive history questionnaire addressed questions on fertility problems to both males and females, separately. The question addressed to the males was limited and used principally as validation of a partner's response. The medical examinations of children were the main sources of information on childhood development, and numbers were limited, especially in the age group under one year.

For these long term effects, the study design consisted mainly of comparisons of incidence between Index and comparison groups, but exposure duration was also a major consideration.

After communications with Dr. J. Evans, human geneticist of the University of Manitoba, verification of reported adverse outcomes by search of hospital and vital statistics records was deferred for inclusion in a proposed Comprehensive Epidemiological Study of Adverse Reproductive Outcomes, whose feasibility is discussed below. Comparison data on the expected prevalence of specific birth defects were sought from the Manitoba Birth Defects Registry.

Our consultants in Medical Genetics and Childhood Development advised us of problems of incompleteness and inconsistencies in reporting of birth defects and congenital abnormalities, in hospital, medical, and vital statistics records, prior to the improvement in Birth Defects Registries about the middle of the 1970's. In many areas these problems still remain, and a separate special prospective study would be needed to ascertain the situation in those institutions in

Southern Alberta where most of these deliveries took place. If a single year historical cohort study of birth defects were feasible despite the small numbers, a year later than 1974 should be chosen for observation. Accordingly, 1985 was selected for the study, and it could be the basis for a future prospective study if one were considered necessary.

Although a large number of individuals exposed to sour gas are included in the study, the incidence of major birth defects in a single year cohort would inevitably be too small for meaningful conclusions to be drawn.

The reproductive history part of the questionnaire inquired about all deliveries in the lifetime of women interviewed in 1985, including those still living within the "exposed" areas, those who had moved out (outmigrants) and those living in the "unexposed" control areas. Histories for older women included pregnancies that occurred before 1957 but problems of recall for events over 30 years ago and other methodologic factors dictated that the major comparisons be for data after 1957. Even so, using data on all the 1985 cohorts pregnancies since 1957 substantially increased the number of reproductive events that could be compared on a cross-sectional basis in terms of woman years of "exposure" to the sour gas emissions against woman years of "non-exposure".

7.1.2 Sampling of Index Subjects

The questionnaire was administered to all respondents in the Index Area, comprising about 93% of those confirmed to be resident there in 1985. The reproductive section of the questionnaire included one question on infertility addressed to males. All the other reproductive history questions were addressed to female respondents, including one on infertility.

Mothers in the Index Area completed a questionnaire for children under one year of age, but only four children of that age were covered in the comparison areas. Questionnaires for children ages 1 - 4 and 5 - 14 were also completed for all respondents in the Index Area and control areas.

Major birth defects and childhood development problems were thus addressed for all Index Area respondents. Medical examinations (ritualistic) were performed on all respondents in the Index Area.

7.1.3 Sampling of Unexposed and Exposed Comparison Subjects

Two areas other than the Index Area were studied. One had a demographically similar population and no exposure to sour gas emissions, the other had exposure to sour gas after 1961 and was demographically different from the Index population. Probability samples were drawn of the residents in these areas in 1985, and they had the same questionnaires administered and medical examinations performed as in the Index Area, except that insufficient numbers of children under one year of age responded to permit comparisons.

Some mothers had pregnancies, in both the "exposed" and "unexposed" areas. Adverse reproductive events were examined in matched pairs of such pregnancies, but their numbers were too small to be useful in this study.

7.1.4 Sampling of Outmigrants

An intensive effort was made to identify individuals who died or moved out of the Index Area since 1957. Telephone and mail questionnaires were used to collect information on adults and children who had moved out of the area since 1957. For the two control areas, information for first degree relatives (siblings or children) and in-laws was obtained.

Criteria for inclusion in the reproductive component was based on years spent in the area since January 1958 in the Index Area and Stirling/Raymond and since January 1961 in DCCI. These dates relate to the beginning of gas plant operations in the Index Area and DCCI.

7.1.5 Types of Data Collected

7.1.5.1 Degree of Exposure

Living in an "exposed" area after 1957 for the duration of the pregnancy is the critical exposure for fetal loss and birth defects. Adverse reproductive results from other known noxious agents, such as rubella virus or Thalidomide, occur after brief exposure very early in pregnancy, so date of conception in an area exposed to sour gas emissions is the time factor that separates the "exposed" from the "unexposed" women. In contrast, alcohol appears to be feto-toxic at any time throughout the pregnancy.

Exposure before or after the first trimester of pregnancy is unlikely to constitute an increased risk of exposure. In any case, if it did, we would not be able to measure it with a study of this type and size. Essentially, we have an "all or none" phenomenon for fetal loss and birth defects.

In comparing prematurity rates between Index and control areas, and between the control areas (SR and DCCI), the subjects in SR were assumed to be never exposed, while those in Index and DCCI were assumed to be exposed throughout the pregnancy.

For infertility and delayed or inadequate childhood development, on the other hand, it may be that prolonged exposure to a noxious agent will be more deleterious than a shorter one. Person-years of exposure is the appropriate denominator for these comparisons.

7.1.5.2 Key Outcome Variables

Four types of adverse reproductive experience data and one type of data on inadequate childhood development, were sought as follows:

Reproductive Experience Data:

1) Fetal Loss
2) Birth Defects
3) Prematurity/Low Birth Weight
4) Infertility/Fertility

Inadequate Childhood Development Data:

1) Height and weight below 5th centile for age;

2) Delayed infant motor development;

3) Denver Developmental Screening test of age 4 years ± 1 month;

4) Delayed sexual maturity in adolescents;

5) Parental dissatisfaction with school progress.

7.1.5.3 Potential Confounding Variables

For fetal loss, four potential confounding variables were measured:

1) Maternal age (1);

2) Pregnancy order and gravidity;

3) Known proximal causes of fetal loss other than sour gas, such as consumption of alcohol and tobacco;

4) Habitual spontaneous abortion.

For birth defects two potential confounding variables were measured:

1) Maternal age;

2) Recent mutation causes of birth defects other than sour gas;

For prematurity and low birth weight , four potential confounding variables were measured:

1) Alcohol consumption; consumers have higher risks of low birth weight babies;

2) Age of mother - <17, >34 years have higher risk;

3) Socio/economic status - lower have higher risk;

4) Marital status - unmarried have higher risk.

5) Tobacco use -

For infertility/fertility estimates, four potential major confounding variables were measured:

1) Use of contraceptives;

2) Attitudes towards family size and spacing, which have changed with time since 1940;

3) Marital status;

4) Religious attitudes to family size.

Data collection in the study took these into account, as discussed in section 7.2.5.

For inadequate childhood development, the potential confounding variables are:

1) Education of parents;

2) Socio/economic status;

3) Birth order;

7.1.6 Contrasts and Comparisons

Except where otherwise noted below, data have been presented in tables with four columns:

1) Index Area - exposed to sour gas emissions;

2) Stirling/Raymond - not exposed control;

3) DCCI - exposed - control for "background" reproductive risks not due to sour gas;

4) Stirling/Raymond minus Mormons - comparison area for DCCI.

The main comparisons is between 1) and 2).

It was considered likely that differences in lifestyle of Mormons might bias results. For reproductive events, specific items discussed under "Potential Confounding Variables" above (section 7.1.5.3) dealt with differences in lifestyle believed to be significant. "Mormonism" per se was not considered a confounding variable in this part of the study.

Some tables include a 5th or 6th column for Southern Alberta, Canada, or some other major source of data outside the study areas.

The women years of exposure were calculated using reported date of in-migration and out-migration and when the emissions of sour gas began.

7.1.6.1 Comparisons of Fetal Loss

Fetal loss is adjusted as the sum of miscarriages plus stillbirths. Miscarriage is used as synonymous with spontaneous abortion. Abortion is used as synonymous with induced abortion.

The rates of fetal loss, expressed as the proportion of the fetal losses to total pregnancies in each area since the year the sour gas emissions began in the exposed areas, were compared among the study areas. Confounding variables (age of mother at time of pregnancy, the dates of occurrence of pregnancies, and the known proximal causes of fetal loss) were controlled for by stratification and/or modelling. The rates for induced abortions, expressed as a proportion of total pregnancies, were compared among the four areas.

The analysis was repeated using rates of fetal loss expressed as the number of women who experienced one or more fetal losses as a proportion of the number of women who had had at least one pregnancy.

7.1.6.2 Comparisons of Prematurity/Low Birth Weight (Questionnaire data)

Proportions of low birth weight babies were compared among the areas. The potential confounding variables (maternal age, alcohol consumption, smoking history, socio/economic status and marital status) were controlled for by stratification and/or modelling. Similar comparisons were also made using the proportion of women who had had one or more low birth weight babies among those with one or more live births.

7.1.6.3 Comparisons of Birth Defects

The proportions of participants in the initial ritualistic medical examination with at least one reported "birth defect", were compared among the areas.

Similarly, the proportions of the same participants determined to have at least one congenital anomaly, were compared among the areas. The proportions of congenital anomalies, stratified by major type and by age group of mother at time of birth, were also investigated.

The proportion of deliveries with birth defects as reported by mothers, stratified by age group of mother, were compared among the areas.

7.1.6.4 Comparisons of Infertility/Fertility

The proportions of men and women who reported fertility were compared among the areas taking into account possible confounders (contraceptive use, attitudes to family size, and marital status).

Fertility rates were compared among the areas taking into account the possible confounders mentioned above.

7.1.6.5 Comparisons of Inadequate Childhood Development

The development of children ascertained by measuring a) the height and weight of all children aged 0-18 years; b) psychomotor development of infants by questionnaire; c) the psychomotor development of children aged 4 years ± 1 month (using the Denver Developmental Screening Test); d) sexual maturity of adolescents (by Tanner Staging); and e) parental satisfaction with the child's school progress.

A composite assessment of development is achieved by using these indicators as follows:

Height and Weight: children aged 0-18 years are considered as having an abnormal height or weight if they are below the 5th centile for age. The standards used are those published in Nelson's Textbook of Pediatrics, 12th Edition, which uses data from the National Centre of Health Statistics, Health Insurance Administration, DHEW, USA.

Infants with delayed development: infants were considered to have delayed development if parents reported that the child could not roll over at 8 months, or sit alone without support at 10 months.

Denver Developmental Screening Test (DDST) Score at age 4 years ±1 month. Items in the 90 percentile category were assigned a value of 1, and those in the category below this were assigned a value of 2. A numerical score for each individual was arrived at by adding the numerical value of the items passed. Comparison between the areas is made by comparing the average score for the population of four year olds in each area.

Delayed sexual maturity in adolescents was defined as follows:

a) In boys: no testicular enlargement by age 13.5 years.

b) In girls: no breast bud development by age 13 years. (Reference: Nelson-Textbook of Pediatrics 12th Edition, p.42)

Parents responding for a child were asked whether they were satisfied or not with their child's school progress.

7.2 Statistical Analysis Methods

7.2.1 Quantification of Key Outcome Variables

The key outcome variables that were selected for this study are now quantified with a view to statistical analysis. For fetal loss, two measures were used:

- proportions of pregnancies leading to fetal loss;
- proportion of women, who had had at least one pregnancy, with one or more pregnancies leading to fetal loss.

For birth defects/congenital anomalies obtained by examination, the proportion of participants with at least one defect identified during examination was the only measure.

For birth defects reported by mothers in the questionnaire, two measures were used:

- proportion of deliveries with birth defects;
- proportion of women, who had had at least one pregnancy, with one or more offspring with birth defects.

For prematurity/low birth weight, the following two measures used:

- proportion of live births with low birth weights (under 2500 gm/5.5 lbs);

Infertility was measured by the following two indices:

- the proportion of women at risk of pregnancy reporting fertility problems in the family, and the proportion of male partners also reporting such problems;
- fertility was also measured by fertility rates in pregnancies per woman-year at risk for females between 15 and 49 years.

Finally, the following five measures were used to assess childhood development:

- the proportion of children below the 5th percentile in height and the similar proportion for weight;
- the proportion of infants with delayed motor development;
- the proportion of adolescents with delayed sexual maturity;
- the proportion of parents dissatisfied with their child's progress at school;
- mean test scores from the Denver Developmental Screening tests performed on all 4 year olds.

7.2.2 Measures of Effect

In the case of continuous outcome measures such as the test scores for the Denver Developmental Screening Test, mean difference was used to assess the effect of exposure. For dichotomous variables, differences of proportions were used to measure the exposure-outcome relation.

7.2.3 Clinical and Statistical Significance

For frequent events, a 20% difference between the exposed and non-exposed populations was considered clinically significant, and 10% for rare events.

An attained significance level of 0.05 was considered statistically significant. Statistical tests were indicated only on differences that were deemed clinically significant.

7.2.4 Effect of Sample Size

The sample sizes for the reproductive study were imposed by the numbers of individuals who were interviewed and/or examined in the overall study. The effect of the sample size could only be assessed therefore by determining the power of the test, that is the probability of detecting a true effect, for a fixed significance level of 5%. These calculations were made a posteriori on each outcome variable and are reported along with the results.

7.2.5 Quantification of the Potential Confounding Variables

The potential confounding variables listed previously were quantified in the following manner for analysis purposes. Note that in order to avoid unnecessary repetitions, these confounding variables are not listed for each outcome variable to which they relate, but all together. The distinction is given in section 7.1.5.

Maternal age - age of mother at time of pregnancy
- year of pregnancy

Pregnancy order and gravidity -

Habitual spontaneous abortion - women with 3 or more spontaneous abortions

Nutrition causes of birth defects - alcohol - never/ever

Alcohol consumption - never/ever

Tobacco consumption - never/ever

Socio/economic status -
- Income - gross family income (< $9,000, $9,000 - 20,000, > $20,000)
- Education - years (≤ 6 years, 7 years - some post secondary, post secondary +)

- Contraceptive use
- Oral contraceptives - never/ever
  - duration and era (years)
- Other types of contraceptives - never/ever
- year of first pregnancy.

Marital status - ever/never married

Other causes - Religion - United
- Catholic
- Mormon
- Other

7.2.6 Statistical Techniques

Classical methods of statistical analysis were used to perform the comparisons. When appropriate, chi-square tests for rates and proportions were used. The corresponding regression techniques have been used to adjust for the potential confounding variables identified. Power calculations, however, have been computed for the crude comparisons only.

8. SPECIAL STUDIES IN HEALTH STATUS EVALUATION

The trace metal and lung function studies, due to their importance and complex methods relative to other aspects of the laboratory measurements, are presented here. The Winter Reassessment, because it was in many ways, distinct from the primary health status evaluation (summer) is also presented separately in this Chapter. The mechanism by which abnormal biochemical and trace metal values were managed is also found in this Chapter because it concerns participant/patient care and not the primary research questions.

8.1 The Trace Metal Studies

Toxicological studies were performed because a proportion of Index Area residents were highly concerned that local trace metal levels were elevated and adversely affecting their health. The choice of which trace metals to measure took into consideration both the wishes of the community and which metals could plausibly be elevated in the area studied. Hair samples were used because they are sensitive indicators of body burden, easily obtainable and transportable. Blood samples were used to measure total mercury, and when necessary, to verify elevated hair levels of lead, cadmium and selenium.

8.1.1 Principal Trace Metal Study

The population and study design have been described in Chapter 5 (Health Status Evaluation). Scalp hair was sampled for determination of mercury, arsenic, lead, cadmium, and selenium concentrations, irrespective of age, when there was an adequate amount of hair. Blood was sampled for mercury in all participants at least 7 years of age.

Accuracy of trace metal results from the Centre de Toxicologie du Quebec was tested as follows: 1) From a 10% simple random sample of participants, hair and blood collections were divided and one portion was sent to the laboratory one week prior to the other portion. The two portions were sent under different identification numbers; 2) From a second 10% simple random sample of participants, hair and blood collection were divided. One portion was randomly allocated to be analyzed by the Centre de Toxicologie du Quebec laboratory and the other was analyzed by the Mayo Clinic laboratory; 3) Human reference hair samples with values certified by the Japanese National Institute for Environmental Studies were sent once or twice weekly to both of the laboratories used in this study. These samples could not be blinded because the hair had been pulverized. The results of accuracy testing are presented in section 9.7. Other quality control measures are described in section 10.2.3.1.

8.1.1.1 Methods

Hair trace metals: participants were instructed to wash their hair before their appointment with a mild shampoo free of additives (i.e., baby shampoo). The use of all shampoos, dyes, tints, and other hair treatments was recorded for each participant. Disposable plastic gloves were worn by the sampler and stainless steel surgical scissors were used. A lock of hair approximately 1 cm in diameter was cut as close as possible to the scalp in the nape area and transported in individual plastic bags. At the Centre de Toxicologie du Quebec, the proximal 1 cm segments of hair were weighed to obtain a total of 40 mg (± 0.1 mg) which was subsequently digested with nitric acid and submitted for atomic absorption with the graphite furnace. Details of the methods are found in Appendix 8.1.1, (Detailed Laboratory Methods).

Blood mercury: after cleaning the antecubital fossa with two alcohol swabs, venous blood was collected in a 10 ml metal-free vacutainer tube (Becton-Dickinson 6527) for blood mercury analysis. Prior to collection, the venipuncture needle was flushed with 7 mls of blood (which was used for biochemistry determinations) to remove any possible metal contaminants. Blood tubes were stored upright, were refrigerated at 4 degrees Celsius within 10 minutes of sampling and were received by the Centre de Toxicologie du Quebec for analysis within 6 days. Mercury determinations were by cold vapour atomic absorption. (Details of methods are found in Appendix 8.1.1.)

8.1.1.2 Analysis

The distribution of hair trace metal values are highly positively skewed for the following two reasons: i) the measured values are commonly very low and close to the lower limit of detection resulting in a very short lower tail of the distribution; ii) hair samples can easily be contaminated resulting in measured values up to 100 fold above the usual values resulting in a long upper tail of the distribution. The arithmetic mean was felt to be a poor measure of central tendency as it would be disproportionately influenced by values in the upper tail and thus have low stability. Therefore, comparisons between areas were done using median values as well as the 5th, 25th, 75th and 95th centile values. In addition, the results were put into the following categories: level undetectable by the Quebec laboratory, level within the normal range for both the Quebec and Mayo Clinic laboratories, level considered high by one laboratory and normal by the other, and level considered high by both laboratories. The values of trace metals defining these categories had been defined *a priori* by each laboratory. Blood mercury values, which are not subject to contamination, would be much less skewed but for consistency and ease of illustration the blood mercury was analysed using the same methods as the hair trace metal results.

Association between categorized results and study areas were tested using a chi-square statistic. The testing of accuracy was done by using percentage agreement and correlation coefficients.

8.1.2 Trace Metal Study of Hutterites

8.1.2.1 Orientation

Hutterites are socially, religiously, and culturally distinct from the general Alberta population. Originating in the Tyrol area of Austria, they migrated first through Europe and then into the United States and Canada. They live together in relatively self-sufficient colonies of about 80 to 150 people, each colony producing and preparing much of its own food locally. Thus, it is possible that their tissue trace metal levels are more influenced by local environmental conditions than those who consume less local produce.

8.1.2.2 Objectives

The overall objective was to study the influence of Hutterite genetic and environmental differences on body trace metal concentrations. The specific objectives were to measure concentrations of blood mercury, and hair arsenic, cadmium, lead, mercury, and selenium in Hutterites; to compare these levels to non-Hutterites living in geographically comparable areas; and to compare the levels between two Hutterite colonies, one living in the Index Area, and one in the Stirling/Raymond area.

8.1.2.3 Study Population

The following two colonies were chosen:

1) The Waterton Colony composed of approximately 95 people living within a few miles east of the Gulf natural gas plant (i.e. Hutterite Index Area).

2) The Cameron Farm Colony composed of approximately 93 people living about 30 miles southeast of Lethbridge (i.e. Hutterite Control Area).

8.1.2.4 Design

Each of the two Hutterite colonies was studied within a 30 day period. In each colony, blood and hair samples were obtained during a two to three hour period from all those currently in the colony. For those who were house-bound, samples were obtained within their homes.

The sampling of trace metals and analysis were as described above in section 8.1.1.

8.2 Lung Function Study

8.2.1 Rationale

The plausible environmental exposures with potential pulmonary toxicity in the Index Area were the oxides of nitrogen (NO_x), sulfuric acid aerosols and sulfur dioxide (SO_2), and hydrogen sulfide (H_2S). The first two are common constituents of atmospheric air pollution and have been inconsistently implicated as causes of adverse effects on respiratory health (Ware et al., 1981; Detels et al., 1981). H_2S is a respiratory asphyxiant in high doses and, in lower concentrations, causes effects similar to those of SO_2 and NO_2; tracheobronchitis and pulmonary edema have been reported (Kurt, 1983). In the context of air pollution, subjects with asthma (characterized by bronchial hyperresponsiveness) may experience bronchoconstriction in response to inhalation of sulfuric acid (Utell et al., 1983) and NO_2 (Orehek et al, 1976) while non-asthmatics are less affected. Therefore, subjects with increased bronchial responsiveness may be particularly at risk of experiencing adverse health effects from exposure to respiratory irritants.

In the present study spirometry was used to evaluate lung function. As compared to other measures of lung function used in population-based studies it is relatively sensitive and specific for respiratory impairment in the context of environmental pollution (Detels et al., 1982). Of spirometric variables, the one-second forced expired volume (FEV_1), was chosen as the primary outcome variable because it reflects airway function, abnormalities of which could be associated with atmospheric pollutants (American Thoracic Society, 1985). The forced vital capacity (FVC) and the mid-maximal expired flow rate (MMEF) were considered secondary response variables. Increased airway responsiveness was measured by response to an inhaled bronchodilator. Results of this test correlate with bronchial responsiveness to histamine, and diurnal variation in peak flow rate (Ryan et al., 1982), and this test has been successfully applied in large population studies (Lorber et al., 1978; Vollmer et al., 1985).

8.2.2 Objectives

The general objective was to determine whether or not residents of the Index Area had poorer lung function than residents in other socio-demographically similar areas of Alberta. The specific objectives were:

1) To determine whether there were differences in mean FEV_1 (FVC and MMEF) between the Index and Stirling/Raymond areas, (the most important contrast.)

2) To determine whether there were differences in mean FEV_1 (FVC and MMEF) between the DCCI area and the Stirling/Raymond non-Mormon population (SR-M).

3) To determine whether individuals with "increased" bronchodilator responsiveness demonstrated an association between exposure level and FEV_1 different from those without "increased" responsiveness.

8.2.3 Study Population

The population and study design have been described in Chapter 5. Pre- and post-bronchodilator spirometry was performed in the sitting position on those subjects over 7 years of age without the following factors which could theoretically increase the risk of the test: age greater than 75 years, pregnancy, diabetes requiring insulin therapy, angina pectoris, past myocardial infarction, history of tachyarrythmias, and clinical hyperthyroidism.

8.2.4 Methods

Spirometry was measured using 8-litre water sealed spirometers with Eagle II microprocessors (Warren Collins Inc., Braintree, Massachusetts). Technicians were supervised by two senior technicians with one and six years of experience in pulmonary research and field studies. FVC was measured as the volume of air expired from total lung capacity to residual volume as defined by a flat line for two seconds duration on the kymograph paper. For each of the FVC and FEV_1 an attempt was made to obtain two or more values within 200cc of the largest. The maximum number of trials allowed for each participant was 8. After the first set of spirometric measurements the bronchodilating agent, 500 micrograms of terbutaline sulfate aerosol (Freedman, 1972), was administered via a Nebuhaler (a 750ml spacer with a one-way valve) (Newman et al., 1984; Newman et al., 1981). Following actuation of the aerosol, participants were instructed to inspire slowly through the nebuhaler from between residual volume and functional residual capacity to total lung capacity and to breath-hold for five seconds. Twenty minutes later spirometry was repeated as described above. Children aged 7 to 12 years were administered only 250 micrograms of terbutaline.

Reproducibility of spirometric results over the summer was tested as follows: from each day of the study a simple random sample of 2-4 participants were selected and these subjects were retested during the last two weeks of August 1985. All retesting was done using one spirometer and the most experienced respiratory function technician. The results of reproducibility testing are presented in section 9.8.2. Other quality control measures are discussed in section 10.2.3.2.

8.2.5. Analysis of Results

Initially, the four groups to be contrasted were compared on factors influencing spirometric results (these results are presented in section 9.8.1).

As recommended by the American Thoracic Society (Ferris, 1978) the largest FVC and FEV_1 obtained from acceptable tracings were used for analysis. The MMEF used for analysis was taken from the spirometric tracing with the largest sum of FVC and FEV_1. Subjects with non-reproducible but acceptable tracings were included in the analysis because poor reproducibility may indicate poor lung function and exclusion of these subjects could therefore cause selection bias (Eisen et al., 1985). Bronchodilator response was measured as the difference between the largest pre-bronchodilator FEV_1 and the largest post-bronchodilator FEV_1. Comparisons between study groups were done on unadjusted values, values expressed as a percentage of predicted by external standards which take into account age, sex, and height (Knudson et al., 1983), and values adjusted by multiple regression analysis for age, sex, height, weight, technician, spirometer used, and cigarette smoking. Lastly the effects of adjusted means were compared between areas by level of bronchodilator response.

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8.3 Winter Reassessment

8.3.1 Rationale

A small proportion of study participants believed that they were less healthy during the winter than during the summer. They suggested that the health status evaluation of the summer may have missed health effects related to season. Supporting such beliefs are these considerations:

1) Atmospheric changes can affect the concentration of airborne pollutants;

2) The cold weather and respiratory illnesses associated with winter may act in an additive or synergistic fashion with environmental pollutants to promote or produce impaired health.

8.3.2 Objectives

The general objective was to determine the extent of seasonal variation on the health status of participants living in the Index and Stirling/Raymond Areas. The specific objectives were as follows:

1) To determine the two week prevalences of respiratory, ocular, cutaneous, neurological, and gastro-intestinal symptoms during the winter.

2) To determine the proportions of participants with current cutaneous, ocular, auricular, or oro-pharyngeal signs of disease.

3) To determine the current level of lung function, as measured by spirometry.

4) For each of the above measurements, to compare within each individual the change between summer and winter.

5) To compare the magnitude of these individual changes in the Index Area to those in the Stirling/Raymond Area.

8.3.3 Study Population and Sample

The eligible study population was defined as all residents from the Index or Stirling/Raymond area, 14 years of age and over who had been study participants during July and August 1985. From this population a random sample of 225 participants was selected from each of the two areas.

The impact of this sample size on the aim of the winter assessment study was evaluated on the basis of a dichotomous outcome and a pessimistic response rate of 2/3 (n = 150). We found that, using McNemar's test statistic with alpha = 0.05, we could detect a difference in proportions of at least 10% between summer and winter with powers of 0.75 and 0.90 depending on the total percentage of discordant results (33% and 22%). Based on these calculations, we felt that the sample size of 225 would be sufficient to attain the objectives stated.

8.3.4 Methods

An abbreviated version of the summer questionnaire was administered by a trained interviewer. A version of the summer ritualized physical examination, abridged to include only the head, neck, and thorax, was performed by a physician who had worked in the summer study. Pre-bronchodilator spirometry was done by two trained technicians. The equipment calibration and methods of testing were identical to the summer study. (The winter questionnaire and physical examination form are in Appendix 10.1). Household heating sources had been ascertained during the summer study.

8.3.5 Analysis

For dichotomous outcomes, the differences between summer and winter proportions were examined using McNemar's matched pairs test. For continuous lung function parameters, the mean differences were compared using a matched-pairs t test.

In both cases, a differential effect of season between the two areas was tested using the IA/SR difference of the winter/summer differences. This comparison, however, was made only after the similarity of the participants in the two areas was established with respect to the same baseline covariates already discussed elsewhere.

9. METHODOLOGICAL RESULTS

9.1 Orientation

This chapter focuses on methodological considerations rather than on the target outcomes or the dependent variables of interest defined in the protocol and the preceding methods chapters. Here we examine the similarity of the samples of participants on the baseline characteristics. We present data about the performance of the research team. We give information about the presence or absence of systematic error or bias that might have complicated interpretation of the main results.

This chapter also marks the beginning of the frequent use of abbreviations and illustration codes to depict the four groups of people compared within Alberta, one reference group from an unexposed control in the Junction Triangle Study of Toronto, selected population groups assessed by the Canada Health Survey, and census data for Southern Alberta. The Junction Triangle unexposed control area is a probability sample of an urban Canadian population in Toronto unexposed to any known environmental risk factors relevant to health. That control area served as the main comparison group for the Toronto Junction Triangle Study that explored the health of residents in a heavily industrialized area in the western part of the City of Toronto. When available, the urban unexposed control area results are given for questions concerning health in the environment. These questions are identical to those posed in Alberta.

These comparisons are simply to assist in interpretation, to give an idea of the order of magnitude of the problems and to give an idea of any differences that might be explained by rural-urban differences alone.

Figure 9.1/1 summarizes the abbreviations which are employed throughout the tables and figures of the remainder of this report.

Figure 9.1/1

SUMMARY OF ABBREVIATIONS AND CODES EMPLOYED IN THIS FINAL REPORT

Abbreviations

IA	Index Area - main area of interest
SR	Stirling/Raymond - unexposed control area which is the main comparison area with IA
DCCI	Didsbury-Carstairs-Crossfield-Irricana-exposed control area
SR-M	Stirling/Raymond minus Mormons - a sub-group of Stirling/Raymond designed as a comparison to DCCI
IA(MC)	Index Area outmigrants - most comparable to outmigrants from SR and DCCI. This consists of first degree relatives only from the Index Area outmigrant respondents
TC	Toronto Control from the Junction Triangle Study - this is the unexposed control area from this study
CHS	Canada Health Survey - data is from 1978-1979 Statistics Canada Health Survey and figures quoted are for all of Canada except where otherwise specified
SA	Southern Alberta, south of an east-west line running through Edmonton but excluding the Calgary and Edmonton census metropolitan areas (see section 4.2.7)

9.2 Comparability of Samples in Areas Contrasted

9.2.1 Selected Sociodemographic Variables

In the following three tables, we characterize the samples drawn from the three areas contrasted in the crossectional survey. Most of the attributes compared were also used by the demography/geography consultant to select the control areas before we went to the field.

9.2.1.1 Selected Sociodemographic Variables Among Adults

Table 9.2.1.1/1, shows a striking similarity between the IA and SR in most variables. The differences in means are small. The IA population is somewhat older, which would tend to produce health status findings that are more adverse for the IA than for the SR. For most variables DCCI and SR-M groups are similar. The urban unexposed sample in Toronto was not very different. In the variables where comparisons can be made, all our samples were similar to Southern Albertans according to the 1981 Census.

TABLE 9.2.1.1/1

SUMMER 1985 SAMPLES*
SELECTED SOCIO-DEMOGRAPHIC VARIABLES
ADULTS
(15 Years and Older)

	AREA					
	IA	SR	DCCI	SR-M	TC	SA
N	1390	485	366	290	261	526584
Percentage female	48.9	46.6	52.2	46.2	50.2	
Population by age:						
15-64	85.4	90.9	84.2	92.4		86.3
65+	14.6	9.1	15.9	7.6		13.7
Mean age	42.0	39.4	42.7	39.4	41.4	
Family income:						
% not reporting	16.3	17.5	19.4	19.7		
% for those reporting:						
- under $9,000	5.2	6.0	2.7	4.5		
- $9,000 - $20,000	19.5	14.9	12.3	12.8		
- $20,000 +	59.0	61.7	65.6	63.1		
Education:						
% not reporting	0.2	1.4	0.6	2.1		
% for those reporting						
- 6 years or less	2.2	2.3	1.4	3.5	23.0	
- 7 years to some post-secondary	74.8	70.7	75.7	71.0	63.0	
- post-secondary or higher	22.8	25.6	22.4	23.5	14.0	
Occupation:						
Farmer	28.3	25.4	19.4	26.7		20.5
Other	71.7	74.6	80.6	73.3		79.5

* Except for TC and SA obtained from other sources.

9.2.1.2 Selected Sociodemographic Variables Among Children

The gender and age of children in the study are presented in Table 9.2.1.2/1. The samples in IA and SR are quite similar. There are many more older children in SR-M than in DCCI, requiring verification and possible adjustment for age in some of the analyses. However, the mean age for all children was similar across the four samples.

9.2.1.3 Other Sociodemographic Variables

There are no differences of practical importance among the four areas in length of occupancy of the current house and length of residence in the area (Table 9.2.1.3/1), except for a tendency of median length of residence for Index Area people to be somewhat higher. However, this is just a slight trend and probably not sufficiently large to require any adjustment.

IA and SR are very similar with respect to family size, but there is a tendency toward a larger number of people from families of six or more in SR-M than in DCCI. IA and SR have similar distributions of religious preference. Mormons form approximately half the sample in each of these areas although more in IA than SR. The data show more Catholics in SR-M than DCCI, and the opposite for membership in the United Church. We

TABLE 9.2.1.2/1

SUMMER 1985 SAMPLES
SELECTED SOCIO-DEMOGRAPHIC VARIABLES
CHILDREN
(0 - 14 years)

	AREA					
	IA	SR	DCCI	SR-M	TC	SA
N	762	343	265	170	108	179292
Percentage Female	48.3	53.1	50.6	48.8	52.8	
Population by age:						
0 - 4	30.8	33.5	40.4	17.1		33.9
5 - 14	69.2	66.5	59.6	82.9		66.1
Mean age	7.1	7.2	6.4	8.2	7.5	

TABLE 9.2.1.3/1

SUMMER 1985 SAMPLES
OTHER SELECTED SOCIO-DEMOGRAPHIC VARIABLES

	AREA			
	IA	SR	DCCI	SR-M
N	2157	839	632	471
Family Size				
1 person	5.1	3.2	5.1	4.0
2 - 5 people	65.3	59.5	84.2	68.2
6+ people	29.5	30.8	9.5	19.1
Other	0.1	6.6	1.3	8.7
Religion				
United	14.2	5.0	29.1	8.9
Catholic	14.3	16.6	15.4	29.5
Mormon	50.1	43.9	0.8	0.0
Other	21.4	30.4	53.2	54.1
Unknown	0.0	4.2	1.6	7.4
N	1428	508	371	302
Occupancy				
≤ 2 Years	19.2	16.6	19.5	17.9
Mean	13.7	11.7	10.7	11.4
Median	9.0	9.0	7.0	8.0
Length of Residence in the Community (in years)				
Mean	26.7	22.9	23.4	21.4
Median	21.0	17.0	17.0	17.0

are unaware of differences between adherents of these two religions that have a bearing on the health-related questions of the study.

9.2.2 Lifestyle Factors

Table 9.2.2/1, gives information on smoking and alcohol consumption. These distributions are seen to be similar for IA vs. SR and for DCCI vs. SR-M. IA residents appear to follow slightly healthier lifestyles in these respects than SR residents; these differences could be due to minor differences in the proportions of Mormons. There is a definite tendency for healthier lifestyles among all Southern Albertans than was found in the Canada Health Survey.

9.2.3 Occupational Exposure to Risk Factors Potentially Hazardous to Health

Exposures in the work place hazardous to health, especially among those working for more than one year, could be confounders of appreciable importance affecting the health outcomes of interest of this study. Table 9.2.3/1 shows that in this study, reported occupational factors were similar between IA and SR and between DCCI and SR-M.

TABLE 9.2.2/1

SUMMER 1985 SAMPLES
SELECTED LIFESTYLE FACTORS
(15 Years and Over)

	AREA				
	IA	SR	DCCI	SR-M	CHS
N	1390	485	366	290	17492
Smoking %					
Never Smoked					
Male	60.1	54.4	44.0	42.3	23.1
Female	74.4	68.1	51.8	59.7	38.3
Combined	**67.1**	**60.8**	**48.1**	**50.3**	**30.8**
Former Smokers					
Male	23.2	23.9	25.7	29.5	27.0
Female	10.9	9.3	18.9	8.2	18.2
Combined	**17.2**	**17.1**	**22.1**	**19.7**	**22.5**
Current Smokers					
Male	15.5	21.6	29.2	28.2	44.1
Female	14.4	22.1	28.8	32.1	37.0
Combined	**15.0**	**21.9**	**29.0**	**30.0**	**40.5**
Alcohol Consumption %					
Occasional & Non Drinkers					
Male	59.2	49.8	36.6	31.4	21.0
Female	71.6	71.2	49.2	59.0	39.3
Combined	**65.3**	**59.8**	**43.2**	**44.1**	**30.3**
Less than 7 drinks/week					
Male	20.0	25.9	30.3	34.6	31.7
Female	20.0	21.2	39.3	28.4	36.2
Combined	**20.0**	**23.7**	**35.0**	**31.7**	**33.9**
More than 7 drinks/week					
Male	19.6	22.4	32.6	30.8	36.5
Female	6.5	7.1	11.0	11.9	14.2
Combined	**13.2**	**15.3**	**21.3**	**22.1**	**25.2**

TABLE 9.2.3/1

SUMMER 1985 SAMPLES
REPORTED OCCUPATIONAL EXPOSURE TO RISK FACTORS POTENTIALLY HAZARDOUS TO HEALTH FOR MORE THAN ONE YEAR
(14 Years and Older)

	AREA			
	IA	SR	DCCI	SR-M
N	1430	508	371	302
Noise	39.0	37.2	42.3	39.7
Dust Particles	37.6	39.4	37.2	43.1
Chemicals or Solvents	23.2	25.4	28.8	26.5
Gas, Chemical Fumes or Smells	22.6	20.9	28.0	22.5
Persons Reporting "Yes" to All Factors Above Except Dust	12.2	10.6	14.3	12.0

9.2.4 Residential Exposure to Risk Factors Potentially Hazardous to Health

There were major differences in distributions of residential exposures (Table 9.2.4/1). Except for gas or chemical fumes, which are directly related to the exposure under study, the differences in the type of water supply, source of food, and type of home insulation are important and required verification by adjustment in the final analysis for certain variables.

9.2.5 Exposure to Pesticides and Herbicides

The use of pesticides near the place of residence could affect the rates for many of the clinical variables, especially in the respiratory system and skin abnormalities. The distribution of pesticide use is different among the areas (Table 9.2.5/1). This required verification of the effect by adjustment.

9.2.6 Selected Sociodemographic Variables Among the 1970 Cohort

In Table 9.2.6/1 we examine sociodemographic variables for the 1970 cohort. This cohort consists of the subsets of the outmigrant and summer 1985 participant population who lived in

TABLE 9.2.4/1

SUMMER 1985 SAMPLES
REPORTED RESIDENTIAL EXPOSURE TO RISK FACTORS POTENTIALLY HAZARDOUS TO HEALTH
(14 Years and Over)

	AREA			
	IA	SR	DCCI	SR-M
N	1428	508	371	302
Dust Particles	62.3	62.8	55.3	60.3
Gas, Chemical Fumes, Smells	49.3	13.2	53.9	14.9
Home Water Supply Not Treated	62.2	16.1	41.0	14.6
Most to Half of Food in Diet Locally Grown	55.7	49.8	43.4	55.0
Fiberglass Wall Insulation	54.1	63.5	64.0	61.5

TABLE 9.2.5/1

SUMMER 1985 SAMPLES DISTRIBUTION OF PARTICIPANTS ACCORDING TO EXPOSURE TO PESTICIDES
(14 years and older)

	AREA			
	IA	SR	DCCI	SR-M
N	1430	508	371	302
Farmers				
- exposed	71.3	91.9	89.7	94.9
- unexposed	13.6	6.5	8.8	3.8
- unknown	15.1	1.6	1.5	1.3
Others				
- exposed	48.3	65.6	63.7	66.8
- unexposed	29.3	33.3	34.7	32.7
- unknown	22.4	1.0	1.7	0.4

TABLE 9.2.6/1

1970 COHORT SOCIODEMOGRAPHIC CHARACTERISTICS

	AREA			
	IA(MC)*	SR	DCCI	SR-M
N	1259	428	338	252
Percentage Female	47.4	45.8	56.8	46.4
Population by Age (in 1970)				
0-4	8.7	12.9	7.7	15.1
5-14	23.4	26.5	28.8	25.0
15-64	65.9	59.2	62.3	58.3
65+	2.0	1.4	1.2	1.6
Mean Age	26.9	23.8	26.2	23.4
Length of Residence (in years)				
Mean	20.8	17.7	18.9	15.8
Median	17.0	15.0	15.0	13.5
Religion				
United	16.4	3.0	33.1	5.2
Catholic	16.8	21.0	13.0	35.7
Mormon	44.6	41.1	1.5	0.0
Other	21.3	30.0	42.9	53.8
Unknown	1.0	4.9	9.5	8.3

* Includes outmigrants who are first degree relatives only

the study areas in 1970. As in the summer 1985 samples, the IA is slightly older than SR. This would tend to produce health status findings that are adverse for IA compared to SR. The difference holds true for the DCCI and SR-M comparison as well. Other differences with regard to length of residence and religion are consistent with the summer 1985 sample. The differences are slight in the case of length of residence and in the case of DCCI and SR-M, we are unaware of differences between adherents of the Catholic and United Churches which would have a bearing on the health-related questions of the study.

9.3 Similarity of Adult Outmigrants Responding

For the adult outmigrants who responded, Tabie 9.3/1 shows the distribution of age, gender, religion, and length of residence in the area of interest for the three areas sampled.

In this table, unlike all other outmigrant result tables, we are including results on the entire ascertained adult outmigrant population for the Index Area. If we compare the two IA populations, we see that there is no appreciable difference in their sociodemographic characteristics except for more people in the 65+ age group.

When looking at our main comparisons, however, IA(MC) vs. SR and DCCI vs. SR-M, are very similar and are also quite similar to the characteristics of the summer 1985 samples.

TABLE 9.3/1

OUTMIGRANT RESPONDING SOCIO-DEMOGRAPHIC CHARACTERISTICS BY AREA (15 Years and Over)

	AREA				
	IA	IA(MC)*	SR	DCCI	SR-M
N	1161	597	248	258	131
Percentage Female	58.0	60.3	58.9	60.9	60.3
Population by Age					
15-64	91.8	97.1	99.6	98.5	99.2
65+	8.2	2.9	0.4	1.6	0.8
Mean Age	38.3	35.2	33.4	33.8	34.8
Religion					
United	17.1	11.4	5.7	37.2	10.7
Catholic	12.9	14.6	19.8	13.2	37.4
Mormon	43.2	49.8	47.2	1.2	0.0
Other	21.5	20.6	25.0	43.0	47.3
Unknown	5.4	3.7	2.4	5.4	4.6
Length of Residence (in years)					
Mean	17.3	18.5	18.0	16.2	19.1
Median	18.0	18.6	19.0	18.0	19.5

* Includes outmigrants who are first degree relatives only

9.4 Response to the MDR Project

9.4.1 Response Rates During the Crossectional Survey in the Summer of 1985

At the time the public announcement of the project was made on May 1, 1985, the Principal Investigator indicated that if a 90% response rate was not attained in all three areas, he would consider the results uninterpretable. We show in Table 9.4.1/1 that the goal was achieved and that the response rates were similar in the three areas surveyed. This reduces any concern about systematic error or bias associated either with differential response rates or low response rates.

9.4.2 Winter Reassessment Response

The important goal in the Winter Reassessment component was not a target response rate, but a number of respondents sufficient for valid within-person comparisons. It had been established in advance that a random sample of 150 adults in each of the IA and SR area was required. In fact, as shown in Table 9.4.2/1, we had 163 respondents in the Index Area and 173 in the SR Area. The table also shows that each of the subsamples of the Winter Reassessment were representative of the summer samples from which it was drawn.

TABLE 9.4.1/1

CROSSECTIONAL SURVEY - SUMMER RESPONSE RATE BY AREA

		AREA		
		IA	SR	DCCI
Total Eligible Per Area	N	2328	922	698
Response Rates		92.65	91.00	90.54

TABLE 9.4.2/1

COMPARISON OF WINTER SUBSAMPLES WITH THE SUMMER SAMPLES FROM WHICH THEY WERE DRAWN
(Adults Only)

	AREA			
	IA Summer	IA* Winter	SR Summer	SR* Winter
N	1390	157	485	164
Percentage female	48.9	50.3	46.6	47.0
Population by age:				
15-64	85.4	86.0	90.9	88.4
65 +	14.6	14.0	9.1	11.6
Mean age	42.0	42.4	39.4	39.7
Occupation:				
Farmer	28.3	32.5	25.4	29.3
Other	71.7	67.5	74.6	70.7

* Denominator excludes six 14 year-olds seen in IA in winter and nine 14 year olds seen in SR in winter.

9.4.3 Contact and Success Rates for Outmigrants

As was expected, the contact and success rates for outmigrants, who were approached by mail questionnaire, were much lower than for participants in the summer and in the Winter Reassessment who were invited to come for a personal data-gathering procedure. The combined success rate was 61.0%. The success rates were 62.7% for the Index Area, 52.8% for the SR Area, 60.6% for DCCI. The similarity of the sociodemographic characteristics of the respondents as shown in section 9.3 militates against a bias created by differential response rate. This also favours a conclusion of no bias in the main results in the crossectional survey as a result of selective migration. Detailed summary of these rates can be seen in Table 9.4.3/1.

TABLE 9.4.3/1

OUTMIGRANT CONTACT AND SUCCESS RATE BY AREA
(%)

	AREA		
	IA	SR	DCCI
N	2316	520	442
Contact Rate*	45.3	40.8	42.1
N	3140	625	548
Success Rate**	62.7	52.8	60.6

* Contact Rate Numerator = Outmigrants identified in the outmigrant master list who responded.

Denominator = Outmigrants in the outmigrant master list presumed alive.

** Success Rate Numerator = Outmigrant respondents from among the contactable or verified master list and newly identified outmigrant respondents and people who had lived in the area and who died.

Denominator = Outmigrants from master list and newly identified outmigrant respondents and people who had lived in the area and who died.

9.5 Coding Repeatability Rates

Many of the variables in the study were self-coding. The data-gathering instruments were so designed to avoid errors when converting the data from questionnaires to computerized data files. However, the answers to questions had to be written in an open-ended manner, especially clinical variables. Accordingly, part of the data management involved coding open-ended items from the questionnaires and clinical recording forms used by physicians. Table 9.5/1 shows the repeatability rates we calculated after analyzing the 10% sample that was recoded to check for inter-coder variability. The lowest repeatability rate obtained was 95.1%. The highest was a 99.7% for cytology. We are confident that the coding process did not introduce any bias or distortion in the data analysis.

TABLE 9.5/1

CODING REPEATABILITY RATES(%) FROM DOUBLE CODING CHECKS

		Percent
1.	Occupation	98.2
2.	Medications, health conditions not in international classifications	98.1
3.	Medical coding - Summer	99.2
	- Winter	
4.	Outmigrant questionnaires	99.3
5.	Pregnancy Matrix	99.2
6.	Electrocardiogram	95.1
7.	Spirometry - Summer	95.9
	- Winter	99.6
8.	Cytology	99.7
9.	Denver Developmental Test	98.7

9.6 Telephone Verification of Questionnaire Data

Random verifications of interviews were done by supervisors by telephone a few days after an interview had been completed on the field. Interviewers were aware that this might be possible. The intention was to achieve a greater degree of alertness and concern about errors among all data gatherers throughout the summer and winter exercises. In the Index Area, fifty four verifications were done using five questions per verification. If one takes all variables into consideration, the accuracy rate was 886 per thousand. There was one question, number 67A, inquiring about the number of years a respondent had lived in the community. This question gave inconsistent results or was unreliably ascertained by the interviewers or the verifiers. The rate of perfect replication is 979 per thousand.

In the Stirling/Raymond area, 52 verifications were done, and when one includes all variables, the accuracy was 889 per thousand. If question 67A is excluded, the accuracy rate is 950 per thousand.

In DCCI, 44 verifications were done. Considering all variables, the accuracy rate was 965 per thousand. Excluding question 67A, the accuracy rate was 991 per thousand.

9.7 Trace Metal Study: Accuracy of Measurements

9.7.1 Reproducibility of Results from the Centre de Toxicologie du Quebec Table (9.7.1/1)

Reproducibility of trace metal results from the Quebec laboratory was tested as follows: from a 10% simple random sample of participants, hair and blood collections were divided; one portion was sent to the laboratory a week prior to the other portion. Each of the two portions was sent under a new identification number. The results, based on 59 hair samples and 57 blood samples are presented in Table 9.7.1/1. With the trace metal values grouped into two to three categories as illustrated, the percentage agreement ranged from 88% for hair mercury to 100% for hair cadmium, hair arsenic and blood mercury with values not categorized.

9.7.2 Comparison of Results Between the Centre de Toxicologie du Quebec and the Minnesota Mayo Clinic

The two laboratories were compared as follows: from a 10% simple random sample of participants, hair and blood collections were divided. One portion was randomly chosen to be analyzed by each laboratory and the results shown on Table 9.7.2/1 are based on 346 hair samples and 279 blood samples. Each laboratory

TABLE 9.7.1/1

REPRODUCIBILITY OF TRACE METAL RESULTS FROM THE CENTRE DE TOXICOLOGIE DU QUEBEC. PERCENTAGE AGREEMENT AND CORRELATION BETWEEN DUPLICATE SAMPLES SENT ONE WEEK APART.*

Trace Metal	Categories	Percentage Agreement**
Mercury blood (ug/L)	≤5 >5 - ≤20 >20	100
Mercury hair (ug/gm)	≤1 >1 - ≤5 >5	88
Arsenic hair (ug/gm)	≤1 >1 - ≤10 >10	100
Cadmium hair (ug/gm)	≤5 >5	100
Lead hair (ug/gm)	≤10 >10 - ≤25 >25	92
Selenium hair (ug/gm)	≤1 >1	97

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* From a 10% simple random sample, each participants' hair and blood collection were divided; one portion was sent to the laboratory one week prior to the other portion (with a differen identification number). Results are based on N = 59 hair samples, and N = 57 blood samples.

** Percentage agreement between the first and second measurements categorized.

TABLE 9.7.2/1

COMPARISON OF THE CENTRE DE TOXICOLOGIE DU QUEBEC WITH THE MINNESOTA MAYO CLINIC LABORATORY ON MEASUREMENTS OF DUPLICATE TRACE METAL SAMPLES. PERCENTAGE OF PARTICIPANTS WITH VALUES IN SPECIFIED RANGES ACCORDING TO EACH LABORATORY.*

Trace Metal	Categories	Centre de Toxicologie	Mayo Clinic	Agreement**
Mercury blood (ug/L)	≤5	99.3	100.0	99.3
	>5 - ≤20	0.7	0.0	
	>20	0.0	0.0	
Mercury hair (ug/gm)	≤1	96.5	99.1	97.1
	>1 - ≤5	2.9	0.6	
	>5	0.6	0.3	
Arsenic hair (ug/gm)	≤1	99.1	99.7	98.8
	>1 - ≤10	0.6	0.0	
	>10	0.3	0.3	
Cadmium hair (ug/gm)	≤5	99.7	99.1	98.8
	>5	0.3	0.9	
Lead hair (ug/gm)	≤10	95.4	98.0	96.0
	>10 - ≤25	4.3	1.5	
	>25	0.3	0.6	
Selenium hair (ug/gm)	≤1	96.2	91.6	93.6
	>1	3.8	8.4	

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* From a 10% simple random sample, each participants' hair and blood collection were divided, and one part randomly chosen for each laboratory for analyses. Results are based on 346 hair samples and 279 blood samples.

** Percentage agreement not corrected for chance.

reported approximately the same proportion of these results to be in each of the categories shown on Table 9.7.2/1. Percentage agreement between the two laboratories ranged from 93.6% for hair selenium to 99.3% for blood mercury.

9.7.3. Calibration of Toxicology Laboratory Measurements by Reference Human Hair

Measurements from both laboratories were calibrated through the months of July and August as follows: human reference hair samples with values certified by the National Institute for Environmental Studies of Japan were sent once or twice weekly to each of the two laboratories throughout July and August 1985. Table 9.7.3/1 shows that both laboratories measured hair cadmium and selenium close to the certified values. The principal laboratory obtained the same results for hair lead as the certified values but the verification laboratory obtained results lower by 3.6 mg/g on average. Both laboratories measured hair mercury lower than the certified value with the principal laboratory being closest.

TABLE 9.7.3/1

COMPARISON OF THE PRINCIPAL LABORATORY AND THE VERIFICATION LABORATORY MEASUREMENTS OF JAPAN N.I.E.S. HAIR WITH ITS CERTIFIED VALUES

Trace Metal	Certified Values	Principal Laboratory (mean, SD)	Verification Laboratory (mean, SD)
Cadmium	0.20	0.2 ±.03	0.21 ±.02
Lead	6	6.0 ±.4	2.4 ±.5
Mercury	4.4	3.9 ±.3	2.0 ±.3
Selenium	1.4	1.0 ±.5	1.1 ±.2

Definition of abbreviation: N.I.E.S. = National Institute for Environmental Studies

Japanese reference material was sent to the Principal laboratory (N = 26) and the Verification laboratory (N = 8) once or twice weekly throughout July and August of 1985.

9.8 Spirometry: Accuracy

9.8.1 Similarity of Areas on Factors Influencing Spirometric Results

The differences (between areas) in distributions of variables that affect lung function are shown in Table 9.8.1/1. Differences in distributions that might increase the level of lung function in the IA compared to the SR Area were as follows: greater heights for both males and females, a smaller proportion of current smokers, and a larger proportion of those that had never smoked. Differences that might increase the lung function in the SR as compared to the IA were the greater proportion of males and younger age among both males and females. There were also differences in distributions between the two areas among pulmonary function technicians and spirometry machines, the effects of which could not be predicted without further analysis. Differences in distributions of variables that would increase the level of lung function of the SR-M as compared to the DCCI group were as follows: the greater proportion of males, younger ages among both males and females, the smaller proportion of current smokers, and the larger proportion of those who had never smoked. Differences between DCCI and SR-M for pulmonary function technicians and spirometers used were much smaller than the differences between the IA and SR group. This may be because the

TABLE 9.8.1/1

COMPARISON, BY AREA, OF VARIABLES INFLUENCING SPIROMETRIC RESULTS*

VARIABLE	AREA			
	IA	SR	DCCI	SR-M
N	1774	653	436	396
Sex Ratio (F/M)	.94	.91	1.0	.84
Age				
Male (mean years)	35.0	32.0	33.6	31.6
Female (mean years)	34.5	30.1	35.0	29.6
Height				
Male (mean cm)	170	168	168	167
Female (mean cm)	160	158	158	159
Weight				
Male (mean kg)	70.8	69.9	69.5	68.2
Female (mean kg)	62.7	59.5	60.1	58.2
Smoking Status (% of Participants)				
Current Smoker	14.6	19.8	29.1	27.4
Ex-Smoker	16.7	16.9	21.2	19.7
Never Smoked	68.0	62.9	48.8	52.6
Technician (% of Tests)				
# 1	30	13	17	15
# 2	07	20	16	17
# 3	32	24	24	24
# 4	22	24	24	26
# 5	09	12	16	13
# 6	00	07	05	05
Spirometer (% of Tests)				
# 1	06	14	17	11
# 2	20	24	24	26
# 3	32	24	24	24
# 4	31	13	17	15
# 5	11	01	00	00
# 6	00	24	18	23

* Variables calculated from those participants with spirometric values available for analysis

DCCI and SR-M measurements (done in August) were done after the technicians had acquired much experience both with techniques and with handling the spirometers.

9.8.2 Reproducibility of Spirometric Results Over the Duration of the Study

From each day of the study a simple random sample of 2-4 participants was chosen and retested during the last two weeks of August 1985. All retesting was done using one spirometer and done by the most senior pulmonary function technician. The results shown in Table 9.8.2/1 are based on 225 participants. The correlation between initial and repeat testing varied from 0.92 to 0.99. The primary outcome variable FEV_1 showed a .3% mean decrease from the initial to the repeat test, with changes varying from -0.2% to -1.3% from June to August. The MMEF was -6.7% on average lower during the repeat testing, ranging from -10.6% to those first tested in June to -4.5% for those first tested in August. The FVC showed a mean increase 1.9% from the first test to the second test, varying from +4.3% in June to -0.3% in August.

Over the summer, the primary outcome variable FEV_1 changed on average less than 1/2% while the second most important outcome variable for spirometry, FVC, changed on average 1.8% with the largest change during the month of June. The reduction in MMEF on the second test tended to follow the increase in the FVC in the second test.

TABLE 9.8.2/1

REPRODUCIBILITY OF SPIROMETRIC RESULTS OVER THE DURATION OF THE STUDY: PERCENTAGE DIFFERENCE AND CORRELATION BETWEEN INITIAL AND REPEAT TESTS*

SPIROMETRIC VALUE	PERCENTAGE DIFFERENCE BY MONTH OF INITIAL TEST			
	Months Combined	June	July	August
N	225	83	78	64
FEV_1	-0.3	-0.2	+0.0	-1.3
	(-.02±.01)	(-.01±.02)	(00±.03)	(-.04±.02)
MMEF	-6.7	-10.6	-4.6	-4.5
	(-.22±.04)	(-.33±.06)	(-.14±.06)	(-.17±.05)
FVC	+1.9	+4.3	+1.0	-0.3
	(+.05±.01)	(+.13±.02)	(+.03±.03)	(-.02±.02)

* Participants initially measured during June, July or August 1985 were re-tested during the last two weeks of August 1985. Percentage difference is defined as the value of the [(second test - first test)/first test] x 100. Absolute difference is in parenthesis with standard error.

9.9 Electrocardiograms: Reproducibility over the Duration of the Study

Reproducibility of the electrocardiographic interpretation over the duration of study was tested as follows: from each testing day during July and August a simple random sample of one or two participants was retested during the last two weeks of August 1985. The results found in Table 9.9/1 are based on 40 participants. Percentage agreement was found to range from 90 to 100% for all categories of abnormality used for analysis in the main study.

TABLE 9.9/1

REPRODUCIBILITY OF ELECTROCARDIOGRAPHIC INTERPRETATION OVER THE DURATION OF THE STUDY. PERCENTAGE AGREEMENT BETWEEN INITIAL AND REPEAT TEST*

Interpretation	Percentage Agreement**
Any abnormality	90
Ectopy	95
Tachycardia Supraventricular	100
Ventricular	100
Atrioventricular blocks	100
Atrial enlargement	100
Intraventricular Conduction defects	95
Ventricular hypertrophy	100
Infarction	98
ST-T wave abnormalities	95

* N = 40 participants initially tested during July and August were re-tested during the last two weeks of August 1985.

** Percentage agreement not corrected for chance.

9.10 Ritualistic Medical Examination Inter-Rater Agreement

A standard videotape presentation of twenty-two physical abnormalities was used to evaluate inter-rater agreement among physicians. The proportion of abnormalities detected by the physicians fluctuated slightly during the summer (Table 9.10/1) but remained high in light of the general experience of abnormality detections in this type of quality control technique.

When one compares the rates of identification of positive signs by the various physicians using six standardized patients, Table 9.10/2 shows visually that there was an acceptable rate of agreement between observers and that the differences among them never attained statistical significance. It is interesting to note that the various physicians, identified by number, elicit a very similar number of signs present as a proportion of all possible signs and that they are sensitive to changes from "less normal" to "more normal" standardized patients introduced through the system.

TABLE 9.10/1

RITUALISTIC MEDICAL EXAMINATION
INTER-RATER AGREEMENT
PHYSICIAN GROUP

	June	July	August
N	4	7	3
Abnormal Items % Abnormal Items Detected	90.1	77.8	81.6

TABLE 9.10/2

RITUALISTIC MEDICAL EXAMINATION
INTER-RATER AGREEMENT - PHYSICIAN EXAMINERS
WITH STANDARDIZED ADULT PATIENTS

Standardized Pt.#1

Examiner #	13	14	17	D.F.	Chi Sq.
Sign not present	90.9	91.7	92.4	2	2.16
Sign present	9.1	8.3	7.6		

Standardized Pt.#2

Examiner #	4	6	7	9	14	D.F.	Chi Sq.
Sign not present	99.2	98.0	97.5	98.9	98.3	4	4.35
Sign present	0.8	2.0	2.5	1.1	1.7		

Standardized Pt. #3

Examiner #	6	8	14	15	16	D.F.	Chi Sq.
Sign not present	95.5	94.9	97.8	95.6	94.3	4	6.41
Sign present	4.5	5.1	2.2	4.4	5.7		

Standardized Pt. #4

Examiner #	9	11	D.F.	Chi Sq.
Sign not present	94.5	94.5	1	0
Sign present	5.5	5.5		

Standardized Pt. #5

Examiner #	4	6	12	16	17	18	D.F.	Chi Sq.
Sign not present	95.1	94.0	95.6	95.9	95.9	95.2	5	2.11
Sign present	18	22	16	15	15	19		

Standardized Pt. #6

Examiner #	3	8	13	15	D.F.	Chi Sq.
Sign not present	93.1	95.2	95.0	95.0	3	2.22
Sign present	7.0	4.8	5.0	5.1		

9.11 Conclusions on Methodological Results

We conclude that the similarity of the groups being contrasted was high, both for the samples assembled in the main crossectional survey in the summer of 1985 and for the outmigrants who responded to the mail survey. The response rates attained the goals set forth in advance and were similar across the areas, both for the summer survey and the outmigrant follow-up. The targets for the Winter Reassessment were met and the subsamples were similar to the samples from which they were drawn and to each other. None of the variables that could have been confounders were sufficiently different among the areas or among the comparison groups to require a statistical adjustment in presentation of the Main Results. This was remarkably so for all the other lifestyle factors and risk factors connected with hazardous exposure in the work place.

In fact, we analyzed the data with statistical adjustment for possible confounders and without adjustment. The differences for most important target outcome variables proved to be negligible if one compares the crude rates with those statistically adjusted. Thus, we feel it has been warranted to conclude that none of the confounders or effect modifiers created bias. Accordingly, we present most of the main results unadjusted, exactly as we ascertained them on the field.

Rates of coding accuracy and spot checks of the ritualistic medical examinations all point to a high rate of quality of performance of the interviewing, medical, and coding staff. Intra and inter-laboratory differences revealed a high percentage of agreement. If the Japanese certified hair samples are considered a criterion or "gold standard", both the principal and verification laboratories provide valid measures of cadmium and selenium and as well the principal laboratory measures lead accurately. Although the hair mercury level was measured low by both laboratories it was low on average by less than 3 ug/gm, a difference of statistical but not clinical significance. In summary, the laboratories, especially the principal laboratory used for the study provided valid measures of trace metals. The comparison by area of variables influencing spirometric results reveals that the distribution of influencing variables are close enough to be amenable to adjustment during the analysis of results in the main study. With respect to reproducibility of the spirometric results, the primary outcome variable FEV_1 shows good reproduciblity throughout the summer months. The FVC was reproducible throughout the summer within approximately 2% with the exception of June, where the initial level was 4.8% lower than the repeat level. This is important because about 1/6 of all Index Area participants and no SR or DCCI participants were measured in June, and therefore some IA results would tend to be biased downward by this finding. If it is found in the main study that the FVC in the Index Area is as good or better than the Stirling/Raymond Area then this finding will not be an issue. The systematically lower MMEF probably relates in part to the change in FVC and the same considerations apply as were discussed with the FVC. In summary the primary outcome variable FEV_1 was proven to be highly reproducible throughout the entire summer and a potential influencing factor was identified for the MMEF and FVC during the month of June.

Electrocardiograms showed excellent reproducibility as expected since they are performed by computerized algorithms. Again ECG abnormalities are relatively rare and this would heavily influence the observed percentage of agreement.

We conclude that the similarity of the groups being contrasted was high, both for the samples assembled in the main crossectional survey in the summer and for the outmigrants who responded to the mail survey. The response rates attained the goals set forth in advance and were similar across the areas, both for the summer survey and the outmigrant follow-up. The targets for the Winter Reassessment were met and the subsamples were similar to the samples from which they were drawn and to each other.

10. SUPPLEMENTARY DETAILED INFORMATION ON METHODS

10.1 Development of Data Collection Instruments

The very broad scope of information required to meet the objectives of the study required the use of a wide range of survey methods and data collection instruments. The major collection methods were based on questionnaires completed by interviewers and on clinical measures, including examination by physicians.

The first of these categories, referred to in the following as the interview component, used four questionnaires, one for people aged 14 and older and three for children according to three age categories.

The second category of data collection instruments, used by physicians, included a protocol for the collection of clinical measures called the "ritualistic medical examination", the "judgemental medical examination" form and the consultant physician form used for referrals. The following sections describe these survey instruments in detail.

10.1.1 Interview Component

The interview component required probing by an interviewer on certain aspects of self-reported acute and chronic health problems, occupational and residential background; lifestyle factors such as smoking habits, past and present, and the use of alcohol, housing conditions, reproductive history, and demographic characteristics. The main objective of the interview component was to derive measures of health status and to examine the interrelationships of the many variables collected within and among the populations of the three study areas.

Different indicators and different data collection techniques were used according to gender and age categories. Four questionnaires were developed. One for adults, intended to capture comprehensive information on certain aspects of health status and on exposure factors related to health, was administered by an interviewer to respondents who were 14 years and older. Three different questionnaires were developed for children to capture information on physical and emotional development as well as on acute and chronic health problems by age groups 0 - 12 months, 13 months to 4 years and 5 - 14 years. All three children questionnaires were systematically administered to the child's mother who served as the proxy respondent.

Since the survey was organized to collect data by household, there was a need to identify all members of the household before data collection. This was the function of the Household Enumeration form, which was completed in a telephone interview at the outset of field activities. For those very few people who did not have a phone, other methods were used to contact them. This was done primarily by getting messages to them through other members of the community.

10.1.2 Health and Exposure Questionnaires

The following illustrates the structure of the questionnaires and provides a rationale for the content of individual sections. Two major considerations were made in determining the structure and content of the questionnaires:

1) The questionnaire should be designed to collect pertinent information for the statistical and descriptive comparisons of target health outcomes in the Index and control areas, as described in section 5.1.6 of this report.

2) Questionnaire items were to be selected from standardized instruments to avoid the long and exacting procedure involved in the development and validation of new research tools. In addition, the use of standardized instruments permits cross-comparisons with readily available data from

other studies, thereby enhancing the interpretation of findings.

As a result of these considerations the adult questionnaire (AQ) incorporated the following:

Section I	Activity status and open-ended probes adapted from items used in the Junction Triangle Study (JTS) (Spitzer, 1984).
Section II	Symptoms relevant to the health concerns of residents of the Index area. Adapted from the JTS.
Section III	Time based disability - items selected from the Canada Health Survey (CHS) (Canada Health Survey, 1981).
Section IV	Drug use - as a proxy for impaired health (CHS).
Section V	Chronic health problems (CHS).
Section VI	Cancer - items selected in consultation with cancer epidemiologists.

Section VII	Chronic respiratory problems - items selected from the 1978 American Thoracic Society questionnaire.
Section VIII	Sociodemographic characteristics (CHS).
Section IX	Occupational background (JTS).
Section X	Residential history and environmental exposure factors (JTS).
Section XI	Mental health symptoms - scale items taken from the instrument used in the Quebec Health Survey (Kovess, 1985).
Section XII	Reproductive history - items selected in consultation with Dr. R. H. Ward, Human Geneticist of the University of British Columbia.

10.1.3 Rationale for Content of Children Questionnaire

The children's questionnaires included items assessing physical health for children aged 0 - 13, social health (ages 5 - 13), general health ratings (ages 0 - 13), and potential satisfaction with development (ages 0 - 4). Other items such as drug use, symptoms, respiratory illnesses, and cancer were adapted from those used in the adult questionnaire.

Physical Health Measures

Physical health measures for children focused on limitations in the performance of a variety of specific daily activities such as physical activities (e.g. walking), mobility, and role activities (e.g. school work).

These functional status items for children aged 0 - 4 were intended to measure two categories of limitations: 1) physical activity, and 2) role activity.

The three role activity items were to ascertain limitations in kind or amount of ordinary play, ability to take part in ordinary play, and ability to do anything the child wants to do.

The questionnaire items regarding functional status for children aged 5 - 13 consisted of two categories of limitations: 1) physical activity, and 2) role activity.

The physical activity items pertained to limitations in vigorous activities such as running, lifting heavy objects, or taking part in strenuous sports. The role activity items pertained to limitations in school-work, and ability to go to school. When a role activity limitation was reported, the proxy respondent rated the duration as 1) less than 1 month, 2) 1 - 3 months, or 3) more than 3 months.

Social Health: Social health refers to how well the child gets along with other children, with family members, and with teachers.

General Health Ratings: Items pertaining to general health ratings have been defined with respect to time (perceptions of prior and current general health) and with respect to resistance/susceptibility to illness. An attempt was made to balance the scale by including positively and negatively worded items.

Satisfaction with Development: General health was also defined in terms of parental satisfaction with the development of younger children (aged 0 - 4) in four areas of potential interest and concerns: 1) overall physical development, 2) eating habits, 3) sleeping habits, and 4) bowel habits.

The children questionnaires (CQ) included items referring to measures on physical and emotional development adapted from the instruments used in the Health Insurance Study (HIS) (U.S. Department of Health and Welfare, 1980). In addition to the questionnaires, the Denver Developmental Screening Test (DDST) was used for children 4 years old, within a range of two months.

10.1.4 Questionnaire Content and Key Target Outcomes

10.1.4.1 Time-Based Disability - (Section III page 9)*

Physical disability is based on an individual's experience during the previous two weeks. Disability days were recorded if the individual was unable to perform normal activities for all or most of the day. Disability days were categorized as bed-days, major activity loss days and cut-down days. Bed-days and cut-down days at home or in hospital, could be looked at both separately and aggregated. Major activity loss days were asked of those people who had a major activity ie., working, school or housework.

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* This reference and the similar ones which follow in this section refer to the questionnaires which may be found in Appendix 10.1.

10.1.4.2 Health Care Utilization - (Section IV page 12 - 13, Question 15 - 15C page 11 - 12, Question 1 - 4A page 1 - 2AQ.)

Drug use, consultations with health professionals, and the use of health establishments such as hospitals are important proxy measures of the status of health.

Drug Use

To minimize problems of recall, respondents were asked whether they had taken any of 10 categories of drugs listed or any others not specified in the list within the last 48 hours before the interview. If drug use was reported, the respondent was asked whether or not it was taken on the advice of a medical doctor.

Consultations with Health Professionals

When a health problem was reported, respondents were asked whether or not they had consulted a health professional during the previous two weeks. If the response was no, they were also asked to identify the reasons for not seeking advice from health professionals when a health problem was reported.

Use of Health Care Facilities

Information was asked regarding the number of nights spent in a health care facility (hospital, nursing home, or convalescent home) in the last year and the last six months. Six months was asked specifically to check the accuracy of one year recall. One year prevalence was reported in the final results.

10.1.4.3 Prevalence of Major Chronic Irreversible Illness - (Section V page 14).

This section is used as a filter to bring to light all long-term episodic ill-health problems that exist but have not been reported through the other probes. This section is necessary as people may have adapted their lifestyle to their condition and not recognize their chronic or episodic health impairments as problems to be reported. These items report the perceptions of respondents and not clinical diagnoses, though the respondents may of course answer questions on the basis of medical diagnoses.

10.1.4.4 Incidence of Definite Diagnosis - (Section VI page 16 - 17, Section VII page 18 - 28).

Incidence of definite diagnosis refers to chronic respiratory illnesses, eczema, hives, heart disease, hypertension, and cancer. Incidence data on these conditions were recorded in order to examine whether or not residents of the Index Area experience rates in excess to what should be expected.

Respondents were asked whether or not they ever experienced any of a set of symptoms related to chronic bronchitis, asthma, and emphysema. They were also queried to determine onset of illness by asking about their age when they first experienced symptoms and when they were first told by a medical doctor that they had the condition. Respondents were asked whether or not they had ever been told by a medical doctor that they had cancer, and when cancer was reported they were asked to specify the type.

10.1.4.5 Burden of Symptoms

The questionnaire asked about specific symptoms consistent to those that are clinically and biologically associated with environmental pollutants. Respondents were asked whether or not they had experienced any of these in the previous two weeks or in the previous twelve months. Further questions asked about use of medical care (seeing a medical doctor and/or taking medications) and about any seasonal variations. Data on these symptoms are expressed as two-week period prevalence and one-year period prevalence. Comparisons for prevalence rates of symptoms among the three study areas are a key component of the research strategy.

Other Categories of Information:

10.1.5 Demographic Characteristics

Questions are posed in this section to determine the respondent's:

- date of birth
- gender
- level of education
- marital status
- annual income
- religion
- occupational history

Demographic information was used:

1) To verify homogeneity of population composition in order to ensure validity in the comparisons of prevalence estimates;

2) As control data in the study of different aspects of the health status of study areas;

3) To profile health-risk groups.

10.1.5.1 Occupational History

A well documented occupational history of survey respondents was considered crucial to the study. The following is a description of occupational information gathered:

- respondents' main occupation;
- present occupation;
- length of time employed in present;
- if retired or unemployed, length of time employed in main occupation and time since last worked;
- type of business, or industry;
- location of present place of work;
- any work exposure to noise, dust, toxic chemicals, gas or chemical fumes. Its frequency (rare, frequent, constant) and level (mild, moderate, severe).

10.1.5.2 Residential Background and Environmental Exposure Factors

This part of the questionnaire was designed to document the respondents' pertinent residential background and exposure factors such as:

- date of entry into the area;
- total length of residence in area;

- periods of and reasons for absence from area;
- geographic location of respondent's home;
- exposure and level of exposure to dust and chemical fumes in area of residence;
- respondents' perception of factors in area of residence affecting their health;
- type of source of home water supply;
- type of home insulation and heating systems;
- pesticides used for farming and other purposes;
- proportion of food in the family diet grown locally.

10.1.5.3 Lifestyle Factors

Lifestyle factors here refer to health-risk factors associated with behaviors such as smoking and alcohol consumption. These two risk factors have been the subject of rigorous epidemiological research whose results point more and more to the insidious health effects of associated behavior. Information was collected in order to identify individuals exposed to these risk factors and to establish relationships, if any, to other health hazards.

10.1.5.4 Mental Health

The Ilfeld (Kovess, 1985) scale was used as a measure of mental health. This scale measures the frequency of occurrence of 20 psychophysiological symptoms of anxiety and depression. A single score can be derived from responses which are weighted to reflect frequency ("very often", "fairly often", "once in a while", and "never").

10.1.5.5 Major Life Events

These items gathered information about recent stressful experiences related to work history and/or stages in the life of respondents in the preceding 12 month period.

10.1.5.6 Reproductive History

This section obtains information from male and female respondents on their reproductive history. Among items included were:

- difficulties in getting pregnant (including fertility problems reported by men);
- ever being pregnant;
- number of pregnancies;
- outcome of these pregnancies (stillbirth, miscarriages);
- current pregnancy;
- birth defects;
- perinatal mortality.

Data from this section were used to profile the health risks of men and women and to establish any associations with other health hazards for women reporting stillbirths, miscarriages, or birth defects.

10.1.6 Questionnaire Pretest

Field testing of the questionnaires was carried out among 75 respondents in Waterloo, an industrial town of Southeastern Quebec. Implementation of the field testing was done by the 19 interviewers who at this time were completing their training period. Minor changes were made in the questionnaire as a result of this testing.

10.1.6.1 Field-Testing and Fine-Tuning

A careful assessment of the first 200 questionnaires administered in the field provided feedback that justified fine-tuning corrections before these survey instruments were submitted for final printing.

10.1.7 Training of Interviewers and Coders

Twenty-four qualified candidates (19 interviewers and 5 coders) underwent a 10-day training period. Interviewers and coders became familiar with the questionnaires (which they received in advance) prior to the beginning of training. Interviewers practiced amongst themselves and observed or participated in interviews conducted by peers and supervisors. Coders received separate training, but joined the interviewers during training sessions relevant to both.

The interviewers' role was to administer a structured questionnaire under standardized conditions. For the most part, survey questions were structured so as to minimize ambiguity in both the questions posed and answers accepted.

10.1.8 Training Manuals

Training manuals were developed as reference guides to enable interviewers and coders to effectively and efficiently carry out their responsibilities. These manuals were designed to complement training so as to standardize coding and interviewing procedures and techniques and minimize the possibility of interview and coding bias.

10.1.9 Editing and Coding

Interviewers routinely edited their own work. Routine editing was also performed by supervisors to check for completeness, legibility, and consistency of all entries into the questionnaire.

Most questionnaire items called for structured responses, which facilitate coding, and reduce error and cost. Open-ended questions were coded in a systematic way. Health problems reported in open-ended answers were recorded in terms of the respondent's self-reported symptoms and health complaints, not necessarily as medical diagnoses. The Ninth Revision of the International Classification of Diseases [ICD-9] and the International Classification of Health Problems in Primary Care [ICHPPC-2] were used for coding purposes. The latter is a widely used coding system for the information recorded when health problems are reported spontaneously by lay respondents in everyday vernacular language.

10.1.10 Child Growth and Development

10.1.10.1 Denver Developmental Screening Test

The Denver Developmental Screening Test (DDST) was designed to aid in the early discovery of children with developmental problems. This test was included in the study as part of the health status evaluation of children four years of age.

The DDST uses a variety of simple tools and tasks to screen the development of infants and children. The items in the test are divided into four areas: gross motor skills, language skills, fine motor adaptive skills, and personal social skills. An overall score of normal, questionable, or abnormal is given.

This test is standardized and easy for non-professionals to administer. A pediatrician trained and provided on-site supervision for the person who administered this test.

10.1.11 The Ritualistic Medical Examination Protocol

The main tactic for clinical measurement was what we have called the "Ritualistic Medical Examination". This examination was designed to satisfy all the requirements of a high-quality medical diagnostic examination. Yet in order to incorporate the standardization, reliability, and validity essential in rigorous research methods it had to be performed without any of the verbal or historic information which, usually precedes physical examination in clinical practice.

10.1.11.1 Protocol Development

Criteria used to select items to be included in the ritualistic medical examination were whether the examination item:

1) Would be included in a periodic health screen of designated age groups;

2) Addressed clinical problems perceived to be of concern to the community;

3) Evaluated clinical signs that have a known or hypothesized association with heavy metal or air pollutants;

4) Was not being addressed by interview or laboratory investigation;

5) Could be standardized and evaluated with a reasonable degree of objectivity (i.e. not highly dependent on the subjective interpretation of both participant and observer);

6) Could be evaluated within the designated age group and within a maximum of 45 minutes/examination.

On the basis of the aforementioned criteria, separate examination protocols were developed for five age groupings: 0 - 1 yr; 2 - 5 yrs; 6 - 9 yrs; 10 - 18 yrs; and 18 years and over. A sixth form was developed for pelvic examinations, all of which were to be carried out by 1-2 physicians in order to enhance standardization of the procedure and interpretation.

10.1.11.2 Standardization of the Elicitation and Interpretation of Examination Data

In order to reduce errors associated with clinical measurement the following steps were taken to standardize the elicitation and interpretation of physical examination data:

1) The examination items were organized from a time-motion perspective. Items within a similar physiological system were deliberately separated to avoid a "carry-over" bias from items already rated.

2) A Procedures Manual and accompanying videotape were developed to orient examiners to the procedures to be used in the ritualistic medical examination;

3) Descriptors were provided for each item in the examination, outlining what would constitute a 0, 1, 2, 3, or positive response by degrees, an 8, or not observed response, and a 9 or not applicable response in the examination. In this way, a standard interpretation of what would constitute normal and abnormal for each item was provided;

4) A pre-test tape and workbook was developed and used to evaluate physician agreement on selected normal and abnormal

examination items;

5) A ritualistic physician orientation protocol was developed to standardize the manner in which physicians were to be prepared to participate in the survey team.

Field testing in early June led to revisions in the order and number of examination items, the procedure used for the examination, and the rating descriptors. These changes were reflected in revised forms, procedure manual, and orientation videotape.

10.1.11.3 Coding

The examination form was set up to permit direct keypunching of data from the rating scales, to eliminate transcription errors. Codebooks were developed for each form along with a master list of examiner numbers for use in quality monitoring.

10.1.12 The Judgemental Medical Examination Form

This form was designed to contain a summary statement made by a second senior physician who after having reviewed all the data gathered up to that point and then saw the participant. This second part of the medical examination is the judgemental medical examination. The judgemental physician used this form to document his/her conclusions and recommendations as well as any other clinical determinations or inquiry that he/she deemed appropriate. In contrast to physicians doing ritualistic medical examinations, who barely spoke to study subjects, the judgemental physicians were free to elicit as much information as possible from the participants, in the mode of conventional history-taking for diagnostic purposes. They also re-examined significant positives and negatives of the findings that had emerged in the ritualistic medical examination.

10.1.13 The Consultation Form

This form was similar to the one just described but designed to contain a summary statement made by a university-based specialist after seeing a referred participant. Most consultations were arranged at the University of Calgary Health Sciences Centre. Referrals were made by the judgemental physician.

10.1.14 Ethical Considerations

The confidentiality of information collected during the study was a major ethical issue, and several procedures were adopted to minimize the potential problems that concerned residents and public officials. All staff persons without exception were required to sign guarantees of confidentiality.

The investigators stipulated from the outset that any results released to public, government or scientific audiences would be in aggregate form only and would not contain reference to individuals.

A consent form to be signed by participants before taking part in the study clearly stated why each test and procedure was to be done, and who would conduct it, which participants would undergo specific tests/procedures, and the benefits of participating. This form also stated assurance of confidentiality and freedom to withdraw from the study at any point. This consent form was part of the study protocol submitted to and approved by a McGill University Ethics Committee.

As a further protection against unauthorized or compromising dissemination of confidential information, the research group followed these rigorous procedures: i) Names were removed from any survey document containing participant data and kept in securely locked cabinets. ii) While individual participants have the right to know about results of their medical and laboratory procedures, requests to obtain this information are subject to a stringent protocol involving the Registrars of the Colleges of Physician and Surgeons of Alberta and Quebec. This protocol was made public in local newspapers.

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10.2 Quality Control of Data

This section reports on the quality control procedures that were implemented throughout all phases of data collection and data management. The areas of greatest concern in quality monitoring were the laboratory for conventional clinical chemistry, the trace metal studies, and clinical measurements. Other areas of concern were of course the health interview survey and all stages of data processing.

10.2.1 Quality Control in the Health Interview

To enhance the quality of the data collected through the health and exposure questionnaires, the following quality control system was implemented:

- Interviewers were trained to administer the questionnaire in a standardized manner;
- Internal consistency checks were built into the questionnaire to verify the accuracy of data before analysis;
- Completed questionnaires were routinely edited to verify consistency and completeness of the data;
- For 10% of adult questionnaires, a set of items was selected and independently re-coded;

- Telephone verification - between 60 and 90 respondents in each area were recontacted by telephone by a supervisory staff person for verification of selected questionnaire items;
- Standardized patients were used to evaluate the consistency and quality of all data gathering. A standardized patient is a person who is normal or has known objective abnormalities who is specifically trained to describe or act out a standardized patient problem so realistically that the acting is not detected by an experienced physician or interviewer.

To improve performance in field activities interviewers/editors, coders, and physicians were made aware at the time of training that quality control systems would be instituted but they did not know the details. Field staff did not know when a standardized patient would go through the system.

10.2.2 Quality Control of the Ritualistic Medical Examination

10.2.2.1 Orientation

The precision of measurement within the ritualistic medical examination was addressed by: 1) structuring the physical examination protocol to enhance inter-rater and intra-rater reliability; and 2) conducting an ongoing quality monitoring program during the process of data collection. The methods used to enhance standardization among physician raters are described below.

10.2.2.2 Structure of the Examination Form

The examination form specified which items were to be examined and the order of examination by each of the following age groups: 0 - 1 years; 2 - 5 years; 6 - 9 years; 10 - 18 years and 19 years and over. The examination items were ordered to enhance time efficiency of the examination and to reduce the likelihood of 'cognitive carry-over' in rating. Cognitive carry-over is defined as a phenomenon where the rater perceives and rates an item on the basis of the rating of previous items examined. In the context of the physical examination, the probability of cognitive carry-over is increased when items are grouped in conceptually meaningful categories, such as by physiological systems, or when the medical history suggests that certain aspects of the examination might be normal or abnormal (Barrows, Neufeld, Norman & Freightner, 1980). For this reason, the order of the examination avoided the grouping of examination items by physiological systems and the medical history was separated from the physical examination. The interpretation of examination items was standardized by employing an ordinal scale for each examination item. Item-specific scale descriptors indicated what would constitute a rating of 0, 1, 2 or 3 with each item.

The numerical rating of examination items by physician raters eliminated the need for coding thereby avoiding errors attributable to this process in data management.

10.2.2.3 Standardization of Examination Technique

The effects on item rating of differences in examination technique or equipment were reduced by:

1) Prescribing the technique for eliciting and rating each examination item;

2) Documenting the examination technique in a Procedures Manual and on videotape for the purpose of physician rater orientation and subsequent reference;

3) Providing identical examination equipment for all examiners;

4) Initially monitoring the application and rating of the prescribed physical examination technique, through direct

observation in the field by a co-principal investigator or an experienced field physician rater.

10.2.2.4 Standardization of the Rating of Examination Items

Variation attributable to differences among physician raters' interpretation and rating of examination items was reduced by:

1) Pre-testing ritualistic physician's interpretation and evaluation of selected examination items. A standard videotape presentation of twenty-two physical abnormalities was used to evaluate inter-rater agreement. The first group of field physician's ratings was employed as the normative standard, used for the purposes of comparison and development of consensus in interpretation.

2) Developing a "buddy" monitoring system, where the most experienced physician raters were paired with those who were least experienced. Physician pairs were given the responsibility of reviewing each others' forms at the completion of each day of data collection for missing data and for issues arising in the process of item rating. Ambiguities in rating were discussed and resolved through periodic meetings of judgemental and ritualistic physicians.

Decisions were logged in the physician log book for subsequent reference and orientation of new physician raters.

3) Providing a standardized orientation for all new physician raters prior to their start of work in the field. The orientation process was divided into three phases. Phase I included general information about the project, the ritualistic medical examination procedure and forms, the reliability of measurement, and the relevance of reliability to the project. Phase II included a review of the forms, procedure manual, and examination procedure tape followed by the observation and rating of an experienced physician rater in the field. New ritualistic physicians then carried out three practice examinations on each other in order to become familiar with the forms. Issues arising during Phase II were discussed with experienced physician raters. During Phase III the new physician raters completed the problem pre-test tape. Their ratings were recorded, analyzed, and discussed with them. New physicians then performed a complete examination in the field under the observation of a designated ritualistic physician who was identified as the normative standard for the project.

10.2.2.5 Monitoring Interpretation and Rating of Ritualistic Medical Examination Items

10.2.2.5.1 Standardized Subjects

Using standardized patients periodically throughout the project to monitor the consistency among physician raters in the interpretation and rating of examination items. Individuals with stable abnormalities or simulated programmed findings who were outside of the study population were examined by all physician raters, who were blind to their identity. A total of eight standardized patients were examined during the field data collection period, two in the Index Area and the remaining six in the two control areas.

10.2.3 Quality Control of Laboratory Data

10.2.3.1 Trace Metal Collection and Analysis

Laboratory techniques for hair and blood sampling were taught and periodically checked on site by persons from the Quebec laboratory. In addition, an independent site visit was carried out by Dr. Jean-Yves Savoie, chemist of the Institute de Recherche en Sante et Securite du Travail du Quebec.

To verify results from the Quebec laboratory, duplicate hair and blood samples from a 10% simple random sample of subjects were sent to the Mayo Clinic Laboratory (Rochester, Minnesota), where measurements were also made by atomic absorption spectrometry. The duplicate blood was sampled from the same venipuncture site and either the first or duplicate sample was randomly selected for Mayo Clinic analysis. Duplicate sampling for hair was done by taking twice the normal amount of hair, dividing it and selecting one subsample for Mayo Clinic analysis.

To validate results from both laboratories, each laboratory analyzed reference hair samples of known metal composition certified by the Japanese National Institute for Environmental Studies.

To measure inter-batch variation in results from the Quebec laboratory, duplicate samples of hair and blood (obtained as described above) from a 10% simple random sample of participants were shipped to Quebec approximately 4 days later than the first samples.

10.2.3.2 Spirometry

Spirometers were calibrated daily using a calibration rod (Collins). This calibration was verified daily using a 3-litre volume syringe. Microprocessor analysis was verified by manual interpretation of the spirogram from the kymograph paper. To check for spirometer leaks the bell was inflated, the air outlet blocked and the drum revolved for a 60 second interval. Drum speed accuracy was verified by running it over a 60 second interval measured by a stopwatch. Inter-technician variability was measured at least each month during the study as follows: a group of approximately 5 to 6 untrained subjects were tested over a period of one hour by all technicians. The order of testing was such that each technician received the same number of individuals who were performing the test for the first, second or third time. To assess the reproducibility of testing over the summer, 227 participants coming from all testing areas were retested during a two week period in August by a technician blinded to the previous test results. In addition, to control for any inter-technician or inter-spirometry variation, each spirometer and technician tested approximately the same percentage of people in the (SR) area and the DCCI area.

10.2.3.3 Electrocardiography

Electrocardiograms (ECG's) were calibrated daily internally and the computerized electrocardiograph was checked approximately once a month. To determine the reproducibility of the ECG's they were repeated approximately four weeks after the initial test on a simple random sample of 40 people with the technician blinded to the results of the first ECG. (Results of reproducibility testing are presented in section 9.9.)

10.2.4 Quality Control in Data Entry and Coding

The basic approach to quality control for data entry and coding was to, in the case of data entry, enter all data twice and in the case of coding, it was to re-code up to 10% of all data. Discrepancy rates were then determined. Should these rates be unacceptable, measures would have had to have been taken to rectify the problems where they occurred. Should these rates be within acceptable limits, increased confidence in the accuracy of the data would be the result.

The keypunchers did a 100% double entry of all data received to minimize keypunch error by means of a computer comparison. This process resulted in a near zero error rate, confirmed by a secondary result of the verification of computer output data which is described in section 10.2.5. Of all corrections made through this process almost none were a result of errors in keypunching.

Each component of the project collected many individual pieces of information on a participant. All information was processed for key punching. Some data gathering instruments were self-coding, that is, coding was done at the time of examination (as was the case of the ritualistic medical examination form). Some data gathering instruments were coded immediately afterwards from responses given by participants (as in the case of the majority of data in the questionnaire). A large part of the data was coded after the fact by a team of trained coders.

For self coded forms, checks were done for completeness of the information. Discrepancies were rectified in the computer verification process described in section 10.2.5. For the questionnaire information coded by the interviewer, a 100% second edit (or check on transcribed codes) was done. There was also a 10% third edit done by supervisory staff.

For the data which was coded by coders, double coding on a simple random sample of up to 10% was done. The double coding was checked against the original coded forms and errors or discrepancies were recorded. The accuracy rates are reported in section 9.5.

10.2.5 Quality Control - Verification of Computer Output Data

The first step used in this study for maintaining quality control of computer output data was the logging by identification number of all pieces of data entered onto the computer by commercial keypunchers. This logging ensured that there would be a record of all the data we expected to find in our data set on the mainframe computer. The information could then be sent for keypunching. The returned tapes from the keypunchers were then examined to assure that no data was missing.

To further ensure that all data were present in the data base, a complete inventory was done on the microcomputer in conjunction with the manual logging system. This inventory was compared with the data set on the McGill mainframe system to locate any data that may have been erased or may never have been entered in the first place. The large amount of data generated by this project required extraordinary efforts to ensure the completeness of the data set.

Once it was certain that all the data were on computer files, our next steps were, 1) to separate the information belonging to ineligible participants from the complete data set; and 2) to verify that each person who went through the study could eventually be traced to each item of his or her data. During the crossectional survey, each participant was assigned a unique sequential identification number and names were later removed from the results to ensure confidentiality during the analysis. The sequential identification number was, therefore, the key to finding a person's results, and so a very important part of preparing the data for analysis was to rectify any duplicate or incorrect identification numbers.

A frequency distribution of responses for each variable in each data gathering instrument were then generated and frequencies were checked manually for appropriateness and for abnormal values (specific to the type of data being verified). Each of the missing, abnormal, and inappropriate variables which could be located through the frequency distribution were then rechecked to verify that they were in fact the participant's intended response, rather than an error in keypunching or coding. Next, the errors present in the logic of the data had to be generated by computer. A logic error, in this case, meant a variable which did not make sense in view of a participant's previous responses. These variables had to be verified with the hard copy to check whether the participant actually presented an illogical response, or whether errors, in addition, coding, or keypunching rendered the data illogical.

When applicable, comparability of data across two sources of information (i.e. different examinations) was also checked. This could be done only when exactly the same information was gathered in two different places such as date of birth and gender.

These procedures for quality control of computer data were used to prepare for analysis all data collected in the crossectional health survey. The data from the longitudinal survey and the Winter Reassessment were subjected to the same procedures for removing errors and ensuring accuracy. The Winter Reassessment data also had to be verified against the summer data to ensure that the recorded changes in health would be accurate.

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10.3 Methods For Mortality Analyses

10.3.1 Objectives

The major objective of the mortality component of the MDR was to determine whether the mortality experience (as registered by Alberta Bureau of Statistics) during the period 1970 through 1984 among all individuals who were alive and resident in the Index Area any time in 1970, was higher than that which should be expected in sociodemographically similar populations in Southern Alberta during the same period.

It must be stated at the outset that it was not an objective of this study to investigate cause-specific mortality. This was because: a) no specific cause of death other than cancer was identified as being of special concern prior to the study; b) information about cause of death was not available to us from the Alberta Bureau of Statistics for reasons of confidentiality; and c) the study was considered to have inadequate power to investigate cause-specific mortality given the constraints of the size of the population under study.

In many ways, the structure of the mortality analysis is similar to that of the study of cancer risks and outcomes described in Chapter 6. Let us recall from Chapter 6 that the Index Area 1970 cohort is defined to consist of all individuals who were alive and resident within the boundries of the Index Area during the year 1970. As in the cancer incidence study, the mortality experience of the Index Area 1970 cohort is the basis of the mortality study. The null hypothesis is that standardized mortality ratios (SMR) for the Index Area 1970 cohort for the period 1970 through 1984 (standardized using rates from sociodemographically similar populations provided by the Alberta Bureau of Statistics), would be equal to 1.0.

10.3.2 Methods

10.3.2.1 Index Area 1970 Cohort

Methods for the enumeration of the Index Area 1970 cohort have already been described in Chapter 4. In addition, methods for the calculation of person-years of risk experienced by this cohort during the period 1970-84 have been described in Chapter 6. Briefly, person-years of risk were categorized by age group, sex and time interval, namely 1970-74, 1975-79, 1980-84. It must be recalled that a person was considered to be no longer at-risk when he or she either died or migrated out of Alberta. Thus it is person-years of life within Alberta that is the parameter being measured. This definition is valid for the mortality analyses since our data concerning mortality were derived from Alberta Vital Statistics data which allowed us to count only those deaths which occurred within Alberta. This is entirely analogous to the cancer incidence study component of the MDR in which only incident cancers diagnosed within Alberta were utilized in the analyses.

The reader is referred to section 6.1.3 for a more detailed description of the cohort definition and enumeration, and to section 6.2.1 for a more detailed description of the exact calculation of person-years of risk. For convenience, we will use the same notation as in the cancer incidence study: namely, we will refer to the subgroup of the Index Area 1970 cohort consisting of individuals who are still alive and resident within the Index Area as the "Resident Group" (RG) and to the subgroup of the Index Area 1970 cohort consisting of those individuals who have either died or migrated out of the area as the "Outmigrant Group" (OG).

10.3.2.2 Expected Deaths

To obtain the expected number of deaths in the Index Area 1970 cohort during the observation period (1970-84), it was first necessary to derive expected mortality rates from comparison populations.

To approximate the Stirling/Raymond area, and yet have available and stable reference rates, we were compelled to use data from census divisions. To be consistent with the cancer incidence study we used as our first reference area Census Division no. 2 excluding Lethbridge. This area includes the entire SR control area and will be referred to as Reference Area 1 (RA1).

Similarly, for the comparison area DCCI, we chose to use Census Division no. 6 excluding Calgary. This area contains the DCCI control area and is identical to one of the reference populations used in the Cancer Incidence study (see Chapter 15). For convenience, we will refer to this second constructed area as Reference Area 2 (RA2).

For each of these reference areas, we obtained census information from both the Alberta Bureau of Statistics and Statistics Canada regarding the period 1970-84. In addition, we were supplied with age group-specific, sex-specific and year-specific death counts for the period 1970 through 84 for these reference areas. By combining these data, we were able to calculate age group-, sex-, and time-interval-specific annual mortality rates for these reference areas.

By applying the appropriate age group-, sex-, time-interval-specific mortality rates to the corresponding age group-, sex-, time-interval-specific person-years of risk, we were able to calculate the expected number of deaths in the Index Area 1970 cohort based on these two reference areas.

10.3.2.3 Observed Deaths

As noted in section 4.3.4.1, the entire edited outmigrant file was manually linked to the mortality file of the Alberta Bureau of Statistics. Specifically, microfiches were supplied which contained records of all deaths in Alberta from the year

1961 through to April of 1985. Each listed outmigrant was checked manually against this mortality file to determine the vital status of the outmigrant, to confirm any reported deaths, and to determine exact date of death were applicable. This entailed a manual search involving every listed outmigrant and 250,000 death records from the Alberta Bureau of Statistics. For reasons of confidentiality, we were not supplied with causes of death. For each member of the outmigrant group, we were thus able to document whether a death occurred within Alberta and whether it occurred during the observation period, namely 1970-84. This information provided us with the observed number of mortalities. We performed separate analyses both including and excluding those deaths which were reported to us but which could not be confirmed by the records of Alberta Bureau of Statistics.

10.3.2.4 Secondary Mortality Analysis

It must be recognized that the reference areas as discussed above were anticipated to be relatively small in size and to have correspondingly small numbers of mortalities during the observation period. This caused some concern as to the stability of the mortality rates that would be obtained via the methods described above. We chose to utilize mortality rates for the general population of Alberta as well in an attempt to study the mortality experience of the Index Area 1970 cohort. This secondary analysis of mortality was conducted as follows: First, age group-, sex-, and time-interval-specific mortality rates from the general Alberta population were applied to the appropriate

Index Area person-years of risk to obtain the expected number of deaths in the cohort based on Alberta rates. Second, the expected numbers of death and the observed numbers of death were used to generate a mortality ratio for the Index Area 1970 cohort standardized against the general Alberta population. This secondary analysis was carried out to compare the mortality experience of the Index Area 1970 cohort against that of the general Alberta population at large.

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Acid
Deposition
Research Program

THE SOUTHWESTERN ALBERTA MEDICAL DIAGNOSTIC REVIEW

Volume Two

RESULTS

DESIGNED AND EXECUTED BY:
THE McGILL INTER-UNIVERSITY RESEARCH GROUP

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ADMINISTERED BY: ALBERTA GOVERNMENT/INDUSTRY
ACID DEPOSITION RESEARCH PROGRAM

JUNE 1986

SOUTHWEST ALBERTA MEDICAL DIAGNOSTIC REVIEW PROJECT

VOLUME II - RESULTS

by

McGill Interuniversity Research Group
with the Epidemiology Rapid Response Unit
of the Montreal General Hospital

Note

This is the final report of the MDR. In the interests of providing the public with the report at the time of the community meetings, and because of the compressed time frames involved in report production, some typographical or arithmetical errors may exist. Further exhaustive editing is in progress.

The definitive version eliminating any such production errors will be printed by the fall of 1986.

CREDIT AND RESPONSIBILITY

The completion of this Medical Diagnostic Review in Southwestern Alberta and the preparation of this final report in one year is a tribute to the teams of men and women in the inter-university research group co-ordinated by McGill University and our colleagues associated with the Acid Deposition Research Program (ADRP).

The co-investigators and professionals listed in the next pages have earned most of the credit for the timeliness and the quality of this study. Having benefitted from the wise counsel of many senior peers and my staff the responsibility for the conclusions published and for any errors is mine alone.

This document, in two volumes and several technical appendices, has been submitted to The Honourable Mr. James F. Dinning, Minister of Community and Occupational Health and to the Co-Chairmen of the ADRP at Edmonton on June 9, 1986.

My colleagues and I thank the government and the citizens of Alberta for the trust placed in us in helping resolve with them one of the most challenging Canadian problems at the interface of the environment and the health of the public.

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Montreal, June 9, 1986

June, 1986

SOUTHWEST ALBERTA MEDICAL DIAGNOSTIC REVIEW PROJECT

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DEFINITIONS AND FREQUENTLY USED TERMS

ADRP - Acid Deposition Research Program.

A priori - Refers to statements or assumptions or statistical criteria set forth in advance of commencing the field work of the Medical Diagnostic Review Project (MDR); the converse of this term in the report is either post-hoc or a posteriori.

Algorithms - A step-by-step procedure for solving a problem or accomplishing some end; in the clinical context this refers to classification methods or treatment decisions done by pre-determined ground rules.

Biostatistics - Quantitative methods of analysing information about living creatures.

CAB - Community Advisory Boards.

CHS - Canada Health Survey: data is from 1978-79 Statistics Canada Health Survey and figures quoted are for all of Canada except when specified.

Cardinal clinical outcome - The symptoms, signs and diagnoses that are most plausibly associated with the environmental risk factors of concern in the Index Areas.

Clinical epidemiology - The study of determinants and effects of clinical decisions.

Clinical significance - A difference sufficiently great that it is impressive because of its consequences for the health of people; clinical significance takes into account the unavoidable reality of uncontrollable or unforeseeable biases as well as real but trivial differences; clinical significance is referred to as "delta" by many statisticians and in every day language it could be referred to as "the difference that makes a difference".

Clustering - The phenomenon of "bunching-up" of people or events or diagnoses; clustering could be in relation to time (for instance there may be an unusual number of cases of measles within a three-month period in a given location), it could be in relation to geography (there might be an unexpectedly high number of cases of absenteeism from school in one village as compared to surrounding ones); clustering could be in relation to diagnosis itself (even though total mortality due to heart disease might be the same in two areas, one could note a clustering of many cases of heart attack in one community versus another).

Cohort - A group of persons sharing common characteristics at a given point in time and defined by an event such as birth, admission to hospital or residence in a particular location.

Corroborate - In the context of this report, corroboration occurs when in comparisons of DCCI versus SR-M the direction of the difference and the magnitude of the difference observed is similar to differences noted in the comparison of IA versus SR.

DCCI - Didsbury - Carstairs - Crossfield - Irricana, exposed control area, north of Calgary.

Demography - The statistical study of human populations especially with reference to size and density, distribution and vital statistics.

Epidemiology - The study of determinants of health and disease in human populations; it includes the study of incidence, distribution and control of disease in a population.

Etiology - Cause or the study of cause.

Heavy (or trace) metals - Metals found in the environment that could penetrate a person's system to dangerous or toxic levels.

IA - Index Area, or the main area of interest exposed to environmental contaminants of concern. An area of southwestern Alberta in and around the towns of Twin Butte, Glenwood, Hill Spring, Willow Creek and Mountain View.

IA (MC) - Index Area outmigrants most comparable to outmigrants from SR and DCCI, consisting only of first degree relatives from the IA outmigrants respondents.

Incidence Period - January 1, 1970 - December 31, 1984

Incident Cancer - Any cancer occurring in a member of the Index Area 1970 cohort during the incidence period as registered by the Alberta Cancer Registry. (Please note: it is recognized under this definition that only cancers that occurred within the Province of Alberta will be registered and thus be considered as incident cancers.)

Index Area 1970 cohort - The collection of all individuals who were alive and resident in the Index Area during the calendar year 1970.

M - Abbreviation for population of Mormon religion.

MDR - Medical Diagnostic Review, being the formal name of this health study.

Methodology - The study of methods.

Period prevalence - The frequency of disease in a population within a span of time. Expressed otherwise, the prevalence of a particular health state or disease in a population of

interest during a period of time. For instance the number of diabetics in Toronto during one year, or two weeks. (This is to be contrasted with point prevalence which is the frequency of the disease at a given instant point in time).

Person Years of Risk - A measure of the population at risk of becoming diseased or dying during a defined period of time.

Post-Hoc Hypotheses - Hypotheses that were not formally put forward at the outset of a study but that are made only after looking at the data.

Power (to detect differences) - A measure of the strength that a study has to detect differences that are real.

Protocol - The plan of a scientific experiment or treatment recorded in writing before initiating the scientific work.

Reference rate - A measure of the frequency of disease or health-related events in a reference or control area.

RFP - "Request for Proposal".

SA - Southern Alberta, south of an east-west line running through Edmonton but excluding the Calgary and Edmonton census metropolitan areas. (In some assessments Lethbridge and Medicine Hat are also excluded.)

SAB - Scientific Advisory Board (appointed by the Acid Deposition Research Program).

SAG - Scientific Advisory Group (appointed by McGill University).

Signs - Observed phenomena in people's bodies as ascertained by professionally trained clinicians (usually physicians). Signs, like symptoms, are indicators of the possibility of disease but are generally considered to be objective findings in clinical research.

Sociodemographic - Attributes of people referring to vital information such as age and sex as well as social and cultural factors.

Spirogram - An instrument that measures the amount and rate of air exchange in the lungs.

SR - Stirling/Raymond, unexposed control area, south of Lethbridge, which is the main comparison area with IA.

SR-M - Stirling/Raymond minus Mormons, a subgroup found to be the best match for comparison to DCCI.

Standardized Incidence Ratio (SIR) - The ratio of the observed number of incident cancers divided by the number of expected cancers where the latter is obtained by applying to

the Index Area 1970 cohort, age-, sex-, and cohort-specific incidence rates derived from referent populations. (See definition of SMR for the description of a similar ratio applying to deaths.)

Standardized Mortality Ratio (SMR) - A rate which expresses the number of observed deaths in a defined area for a defined period compared to those you would expect if the rates of a reference population (such as an entire province) applied in the area concerned. For instance, if there were 75 observed deaths in a particular area during a decade and one expected 100 deaths in that same area given the provincial rates, the SMR would be 0.75. In situations where there is neither an excess nor a deficit of deaths in a given area the SMR is very close to 1.0 (unity).

Statistical significance - A statement that indicates the likelihood that differences in numbers or rates or averages observed could have arisen by chance alone.

Supplemental Incidence Period - January 1, 1985 - December 31, 1985.

Symptoms - Perceptions which people have about themselves or about their body which are indicators of possible disease. Symptoms are reports of persons as patients as they describe what they feel and are generally considered to be subjective findings.

Toxicology - A science that deals both with poisons and other substances to link their effect with health problems.

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11. RESULTS

11.1 Orientation to Presentation of Results

The presentation of Principal Results does not follow the order of presentation of Methods. The presentation of Methods was set forth in a way that helps understand opportunities and constraints in the field, the chronological sequence of activities and events of the project and the interaction of crossectional and cohort data-gathering tasks. The order for Results has been selected with attention to the logic of the clinical epidemiologic and biologic issues.

It has deserved emphasis, at various points in this Report, that the main research question asked in this project is whether the people exposed to emissions of sour gas in the Index Area have a different health status or health experience than the most similar and unexposed population within the Province of Alberta. The best reference or control population proved to be the residents in the Stirling/Raymond area as described and justified in the Methods sections. Expressed otherwise, the main question of this study concerns a possible "epidemic" of adverse health among people in the Index Area. This study was not intended to explore etiologic or causal significance of association, if any were to be observed. Determining whether there is an epidemic or not requires comparison of the IA residents with the SR area residents. Thus, the majority of our comments about contrasts and comparisons dwell on the Index Area versus Stirling/Raymond (IA vs. SR). Comparisons with the exposed control area, DCCI, and with the Stirling/Raymond minus Mormons (SR-M) sample assist in interpretation or corroboration of the main contrasts. However, there were no prior hypotheses about the ancillary comparisons. Accordingly, the differences or similarities between DCCI and SR-M compared against each other or against IA must be interpreted with greater caution than those between IA and SR. We employ the term "corroboration" in our descriptions and discussion to denote a situation where the contrast DCCI vs. SR-M shows differences or similarities that parallel the contrast between IA vs. SR.

We conclude this section by repeating the codes we have used in the tables of this section on Principal Results to facilitate reading:

Abbreviations

IA	Index Area - main area of interest
IA(MC)	Index Area outmigrants - most comparable to outmigrants from the SR and DCCI. This consists of first degree relatives only from the Index Area outmigrant respondents

SR	Stirling/Raymond - unexposed control area which is the main comparison area with IA
DCCI	Didsbury-Carstairs-Crossfield-Irricana-exposed control area
SR-M	Stirling/Raymond minus Mormons - a sub-group of Stirling/Raymond designed as a comparison to DCCI
TC	Toronto Control from the Junction Triangle Study - this is the unexposed control area from that study done in 1983
CHS	Canada Health Survey - data are from the 1978-1979 Statistics Canada Health Survey and figures quoted are for all of Canada except where otherwise specified
SA	Southern Alberta, south of an east-west line running through Edmonton but excluding the Calgary and Edmonton census metropolitan areas (see section 4.2.7),

11.1.1 Presentation in Chapters 12 through 17

We present tables in groupings corresponding to the key target variables (dependent variables) proposed in the original protocol and the Methods section. When applicable, the specific question in the questionnaire used to gather the data is appended to the table. Each table is followed by a brief descriptive comment avoiding repetition of the tabular content. In some sections (e.g., Cancer and Reproductive Risks and Outcomes) the text is expanded due to the complexity and uniqueness of the methodological issues. For those sections the Methodological Results are with the section (rather than in Chapter 9 or 10) for the convenience of the reader. Interpretation is generally given under Discussion (Chapter 18) and Conclusions (Chapter 19).

11.2 Statistical Introductory Comments

It is important at this point to reiterate the statistical considerations that have been the basis for analytic and interpretation of the data presented in this part of the report.

First, we declared in advance that "clinical significance" would have to be attained in order to consider the two areas under study (IA vs. SR) as different for a given health problem. The level of clinical significance selected *a priori* was a difference in rates of 10% when the reference rate was less than 10% (or larger than 90%), and a difference of 20% when the reference rate was greater than 10% (or less than 90%). In statistical technical terms, these values are called the "deltas" or, in everyday language, "the differences that make a difference". It is important to recognize that these deltas are critical in assessing subjective findings such as reported symptoms. In fact, these deltas are composed of two components: unforseeable or uncontrollable biases and real but inconsequential differences. In spite of the rigour used to eliminate potential biases, we could not alter such realities as fundamental biological (ethnic or other) biases between nonrandomized study groups, variables in the perception of a health hazard that might influence responses to questions about a health problem, or subtle differences in interviewer technique such as a tendency for an interviewer to probe the responses more diligently in one area than another. These are examples of what we call uncontrollable biases in this study. A second component of delta is a real but unimportant or even trivial difference (such as an average difference of blood pressure of 2 mm). When these components are taken into account, we postulated in advance that a "clinically significant difference" is large enough that it cannot be explained either by bias or as a trivial effect or both. Expressed conversely, we would not be prepared to dismiss differences of greater than 10% (when reference rates are below 10% or above 90%). The more objective health outcomes such as laboratory findings have not been subjected to this process. Instead, we deal with each objective variable individually, on the basis of known standards from the literature or the experience of the investigators and consultants.

A second important statistical consideration, related to the first one, is that of statistical significance (p-value). The primary issue is that, because of the use of a large sample of individuals (complete census of the IA), "very small" differences in rates or means (less than the deltas) will be statistically significant by conventional norms. A secondary issue is that, because of the so-called uncontrollable biases, calculated p-values will tend to be lower than with unbiased data. For these reasons, we do not rely solely on statistical significance for inference. Accordingly, p-values are infrequently reported in this study, although we had declared in the original protocol that only significance levels less than 1% would be significant. The changes in sample size from those of the original protocol along with the reasons given above reinforce this requirement.

A third important statistical consideration concerns multiple comparisons. When we set a statistical significance level (alpha) at 5%, for example, we fix the chance of erroneously concluding that IA and SR are different when in fact this is not true (type I error). This means that if IA and SR are equal then, on the average, we will find about five "statistically significant" differences in each 100 independent comparisons that we make. This problem may become very serious when several different measures of health (in our case hundreds) are assessed simultaneously. In this case, the type I error probability increases with the number of measures, so that the probability of this error can become virtually 100% for a few of the measures. For example, if we have 100 health measures in which there is no real effect and we wish to conduct a statistical test for each measure at level 5%, assuming that the measures are independent of each other, then we can compute the probability of finding 1 or more of these measures statistically significant, 2 or more, 3 or more etc. These are given in Table 11.2/1.

TABLE 11.2/1

Number of Statistically Significant Comparisons in 100 Independent Tests	Probability of this Number of Statistically Significant Comparisons
1 or more	99.4%
2 "	96.3%
3 "	88.2%
4 "	74.3%
5 "	56.5%
6 "	38.4%

With 100 or more statistical tests at the usual 5% level, it is virtually certain that some health measures will be statistically significant simply by chance alone. Focussing the attention on a few significant differences would be a mistake since they may well be due to chance. For this reason, we had also stated in advance that 10 to 12 key outcome measures would form the basis of inference in this study. In order to represent as exhaustively as possible the complete health assessment while not including all possible measures on an individual basis, global indices were created. Keeping in mind the problem of multiple comparisons, priority would then be given to these measures and to a much lesser extent to the other secondary results from which these were obtained.

A fourth important statistical issue, related to multiple comparisons, is that of post-hoc hypotheses. It is dangerous to test a hypothesis after the fact, after having seen the data, because of the certainty of finding some significant results solely by chance. Therefore, although tempting, post hoc hypotheses are usually data-driven and have been set aside by our team of investigators.

A fifth statistical consideration is that of the power of the results. Complementary to the significance level alpha, the power of a test is related to beta (power = 1-beta), where beta is the probability that one finds no difference between IA and SR when in fact they are different (type II error). The power is therefore the probability of being able to detect "differences worth detecting". We were able to perform power calculations on the basis of the sample sizes obtained. Conservatively, considering the sample sizes of approximately 1300 and 400 adults in the IA and SR areas respectively, using dichotomous data with an alpha of 1%, the power for detecting differences of 20% or 10%, depending on whether the lower rate is frequent or not, is always at least 99.1%. Note that the value alpha = 1% corresponds to a rate difference of 4% to 7% for adults and 5% to 9% for children (in the range of those observed). In similar calculations for children, sample sizes being approximately 600 and 300 for IA and SR respectively, power levels are at least 92.7%. It would have been difficult to detect smaller differences with enough power from these sample sizes. For example, had we desired to detect differences half the size we specified, namely 10% and 5% respectively for frequent and less frequent subjective outcomes, the power would have been reduced to a range of 57% to 97% for adults and a range of 36% to 84% for children.

The last statistical issue here concerns the presentation of crude instead of adjusted results. Although we made a determined effort to achieve a design that would permit a simple and straightforward strategy of analysis, it is impossible without randomization to obtain a reference group exactly like the study area. The SR area, however, proved to be highly similar. Before deciding whether to present crude results or adjusted results, we performed adjusted analyses that controlled the contrasts for the effect of various potential confounding variables suspected or found to be differentially distributed among the two areas. These variables were: age, sex, occupation, length of residence in the area, religion, smoking behaviour, alcohol consumption, type of home water supply, source of food, type of home insulation, exposure to dust, and exposure to gas and chemicals. The key outcome variables, each aggregated into a global index, were analyzed using logistic regression to produce the results in Table 11.2/2.

These potential confounding variables had only a negligible effect on controllable bias, which justifies the presentation of unadjusted results exactly as they were elicited in the field. Thus the simple unadjusted results remain meaningful with respect to the research questions that we seek to answer.

In order not to clutter the majority of the tables found in the following chapters, percentages of missing data were removed from each table. Where several sample sizes pertain to one

TABLE 11.2/2

COMPARISONS OF CRUDE AND ADJUSTED* RISK (PERCENT) DIFFERENCES BETWEEN IA AND SR FOR 10 KEY OUTCOME VARIABLES (ADULTS)

			Risk Difference	
Reported Findings	IA	SR	Crude	Adjusted
% with at least one symptom in preceding 2 weeks	79.7	74.1	5.6	6.3
% with some activity loss in preceding 2 weeks	21.3	17.3	4.0	7.6
% at least one night in hospital in preceding year	17.8	14.2	3.6	3.9
% at least one chronic illness	21.4	16.0	5.4	1.3
% with at least one health problem	57.4	53.7	3.7	1.0
% Chronic Bronchitis	12.3	8.5	3.8	3.7
Objective Findings				
% Hypertension	12.12	11.69	0.43	0.003
% Myocardial Infarction	1.95	1.27	0.68	-0.005
% Left Ventricular Hypertrophy	1.52	0.85	0.67	.006
% With High Urea	3.67	1.96	1.71	1.07

* Controlling for the potential confounding variables listed in this section.

table, we present only the largest one. The number of missing data is very small in most cases (in the order of 0.5% to 2.0%). There is no alteration of practical consequence from this form of presentation, but clarity gains.

12. OUTMIGRANT FINDINGS RELEVANT TO HEALTH-RELATED SELECTIVE MIGRATION

In this brief Chapter we recapitulate some of the data shown in Chapter 9 and Chapter 16. We also present a few additional tables regarding selected characteristics of outmigrants.

There has always been concern on the part of the Scientific Advisory Board, the Community Advisory Boards and the investigators about possible selective migration out of the Index Area for reasons determined by health. The result of such selective migration could be that residents living in the Index Area in 1985 might appear to be either spuriously healthier or spuriously less healthy than the comparison group in the SR area. Accordingly, there were two reasons for doing the outmigrant follow up. One was to obtain empirical data to help decide if the health-mediated migration patterns out of the Index Area and out of the SR area were different. If that proved to be so, then crossectional comparisons between IA and SR would have to be done very cautiously. Heavy reliance would have to be placed on data pertaining to the 1970 cohorts of IA and SR to settle the questions explored by the MDR. The second important purpose was to follow outmigrants to do ascertainment on cancer incidence and about events surrounding reproduction and birth. Our analysis strategy dictates that our conclusions about the cancer experience in the Index Area and its experience with reproductive risks and outcomes should be based on person-years of exposure beginning either in 1970 or 1957.

12.1 Sociodemographic Characteristics

The reader is referred to Table 9.2.1.1/1, Table 9.2.1.3/1 and Table 9.3/1 under Methodological Results. It will be noted there that outmigrants are younger than those who remained in the geographic area studied, that their distribution by religion was similar to residents who were still in the original area in 1985 and that they had lived less numbers of years in the areas studied. It also suggests that the relative porportions of IA outmigrants and SR outmigrants by sociodemographic variables of interest are similar in magnitude and direction as the corresponding ones for those remaining as residents, especially if one compares IA with SR.

Turning now to Table 16.1/1 and Table 16.1/3 where selected sociodemographic variables of women of childbearing age are shown for summer participants and outmigrant respondents, again the outmigrant women are younger, their religion distribution is similar to that of those who remained in the geographic area of concern. Their length of residence was similar.

12.2 Comparison of Rates of Illness Among Outmigrants and Summer 1985 Participants

In Table 12.2/1 we show the rates of certain illness ascertained among participants in the summer samples of 1985 compared to the rates obtained among outmigrants who had lived in the various areas sometime since 1957.

These findings have to be interpreted with caution for the following reasons: (i) data in the summer of 1985 were gathered by personal interview and those gathered among outmigrants were obtained by mail questionnaires; (ii) the questioning in the summer was more comprehensive with some branching logic, in the mailed questionnaires, by necessity, the process had to be brief; (iii) recall among some outmigrants who had not lived in areas from which they left many years ago could be deemed to be worse than for people who had remained in the area.

Nevertheless, there is a consistent pattern of higher rates of illness for summer participants except for epilepsy and diabetes. Also the ratio IA to SR is similar for the summer 1985 participants and outmigrants in most cases.

In Table 12.2/2 we compare the reasons why outmigrants left the area where they had lived. What we were interested in was the proportion of people who had moved due to health reasons. For all categories of outmigrants the percentage was very low. Taking IA(MC) as the most comparable outmigrant group to the SR outmigrants we show information that must be interpreted remembering that people who move out are younger. The reasons for moving were to seek education, to seek employment or to establish business, for family reasons or to get married. All these predominating reasons are coherent with the fact that younger people moved out. Also, the fact that younger people migrated confirms the observation that they appear to be healthier as reflected in the percentages of illness reported (Table 12.2/1).

TABLE 12.2/1

COMPARISON OF SELF-REPORTED 1985 ILLNESS AMONG OUTMIGRANTS AND SUMMER PARTICIPANTS (PERCENT)
(15 Years and Over)

	IA*	SR	DCCI	SR-M
N Summer	1390	485	366	290
Outmigrants	599	250	264	132
Heart Disease				
Summer	13.6 (13.4)**	11.8 (11.3)	9.6 (9.6)	10.7 (10.0)
Outmigrants	2.3	1.2	1.5	0.8
Hypertension				
Summer	21.1 (20.8)	15.5 (15.3)	23.2 (23.1)	16.6 (16.2)
Outmigrants	5.2	3.2	3.8	4.6
Migraine				
Summer	12.6	8.3	9.3	6.6
Outmigrants	7.4	6.4	4.2	5.3
Epilepsy				
Summer	0.3	0.4	0.8	0.3
Outmigrants	1.7	0.4	1.5	0.0
Chronic Bronchitis of Phlegm > 1yr				
Summer	20.3 (4.3)	13.6 (3.5)	19.1 (5.0)	14.5 (3.8)
Outmigrants	4.3	2.4	1.9	1.5
Chronic Lung Disease (Emphysema)				
Summer	0.8	0.0	1.1	0.0
Outmigrants	1.0	0.4	0.0	0.0
Diabetes				
Summer	2.7	1.4	1.9	1.7
Outmigrants	2.2	2.0	1.1	3.0

* For outmigrants, this area includes only people who are first degree relatives of the contact person.

** Numbers in brackets correspond to summer sample people with a positive response to the direct question "Were you ever told by a doctor that you had (illness names)". This formulation is most similar to that which is asked in the outmigrant questionnaire.

TABLE 12.2/2

OUTMIGRANTS REASON FOR MOVING OUT

	AREA			
	IA(MC)*	SR	DCCI	SR-M
N	599	252	265	132
Health	1.3	0.4	1.1	0.0
Education	40.1	33.7	33.6	33.3
Business/Employment	28.2	26.6	36.2	27.3
Family/Marriage	18.4	20.2	19.3	21.2
Other	7.0	7.5	3.4	7.6
Unknown	5.0	11.5	6.4	10.6

* This area consists of Index Area first degree relatives only

13. HEALTH STATUS EVALUATION

In this chapter we review groups of variables which are conventional indicators of the health status of population. The majority of these are based on information supplied by respondents in the various areas and are, therefore, subjective. Some of them have been verified with data from independent sources.

The first group of health status indicators concern current physical disability as reported by the respondents.

The second group, utilization of health services, must be used only with a great deal of caution as an indicator of health status or as a proxy for sickness and morbidity. That is because the rates of use of health services, including visits to health professionals and use of hospitals and related facilities, are influenced very much by access to and availability of either health professionals or hospital beds as well as patient's demands and beliefs about their own health. While all these effects may be small under Canada's health care delivery system, we cannot assure that they are nil or negligible.

The third group, prevalence of major chronic irreversible disease, answers one of the key questions put by the population and the Acid Deposition Research Program at the outset of this project.

The last group, clinical findings, examines symptoms, signs, laboratory tests, specialist consultations and clinical algorithms. Symptoms are perceived by the population, and as such are subjective in contrast to burden of signs which are observations made by physicians, frequently twice, as independent assessments. Laboratory findings as indicators or as corroborators of diagnosed disease are very important in this project and of great interest to the Community Advisory Boards. Rates of diagnosed disease are ascertained in many ways including confirmation by specialist consultation in a university hospital and as established by formal clinical algorithms.

We have focussed on cardinal outcomes of health. These have been defined in the Methods Chapter and they include the symptoms, signs, and diagnoses that are most plausibly associated with the environmental risk factors of concern in the Index Area. All cardinal symptoms, signs, and diagnoses were declared before the field work was conducted and documented before the analysis began.

13.1 Current Physical Disability

13.1.1 Orientation and Findings

The following tables summarize our findings concerning current physical disability of the participants in the areas compared. We start with summary expressions of current physical disability, then review some of the individual variables used to draw up the composite variables presented in the first four tables. All data in this section are derived from the questionnaire.

In Table 13.1.1/1 we present data regarding physical functional capacity for the various samples. This is a composite variable and there is a 3.9% difference between IA and SR in the percentage of persons free of any activity loss. There is no difference between DCCI and SR-M. The percentages of persons free of bed disability in the preceding two weeks are similar across the four samples.

In Table 13.1.1/2 we examine the same attributes used in Table 13.1.1/1, but this time we report the percentage of days rather than the percentage of persons. Again, there are only small differences across all the samples for both composite variables. Tables 13.1.1/1 and 13.1.1/2 together show that the

TABLE 13.1.1/1

PERCENTAGE OF ADULTS FREE OF ANY ACTIVITY LOSS AND BED DISABILITY IN THE LAST TWO WEEKS
(15 Years and Over)

	AREA			
	IA	SR	DCCI	SR-M
N	1390	485	366	290
% Free of:				
Any Activity Loss	78.4	82.3	82.0	83.5
Bed Disability	92.5	92.6	94.8	93.5

Question 12: DURING THE PAST 2 WEEKS, DID YOU STAY IN BED AT ALL BECAUSE OF YOUR HEALTH?

Question 13: DURING THE PAST 2 WEEKS, DID YOUR HEALTH KEEP YOU FROM ______________________ (ACTIVITY STATUS) AT ALL?

Question 14: (NOT COUNTING THE DAYS MENTIONED EARLIER) WERE THERE ANY (OTHER) DAYS DURING THE LAST 2 WEEKS THAT YOU CUT DOWN ON THINGS YOU USUALLY DO BECAUSE OF YOUR HEALTH?

"Free of any activity loss" is a "no" response to all of the above.
"Bed disability" is a "no" response to Question 12.

TABLE 13.1.1/2

PERCENTAGE OF DAYS FREE OF ANY ACTIVITY LOSS AND BED DISABILITY IN THE LAST TWO WEEKS
(15 Years and Over)

	AREA			
	IA	SR	DCCI	SR-M
N	1390	485	366	290
% of Days Free of:				
Any Activity Loss	93.3	93.1	95.1	94.5
Bed Disability	98.9	98.5	99.2	99.2

Question 12A:	HOW MANY DAYS DID YOU STAY IN BED FOR ALL OR MOST OF THE DAY, INCLUDING ANY NIGHTS SPENT AS A PATIENT IN A HOSPITAL?
Question 13A:	HOW MANY DAYS DID ILLNESS OR INJURY KEEP YOU FROM ________________ (ACTIVITY STATUS) FOR ALL OR MOST OF THE DAY?
Question 14A:	AGAIN, NOT COUNTING THE DAYS IN BED AND DAYS LOST FROM ________________ (ACTIVITY STATUS), HOW MANY DAYS DID YOU CUT DOWN FOR ALL OR MOST OF THE DAY?

"Free of any activity loss" is the sum of all three questions. "Bed disability" is the number reported in question 12A.

percent of persons with any activity loss was slightly (and nonsignificantly) higher in IA than in SR, but the duration of such loss was on average shorter in IA than in SR, to give virtually identical mean days of activity loss.

Table 13.1.1/3, shows the percentage of persons free of major activity loss among those normally occupied with school, housework, or work outside the home. The percentages for IA are similar to those for SR.

In Table 13.1.1/4 we examine the proportion of days free of major activity loss in the last two weeks, again restricted to those whose activity status was school, housework or working outside the home. No differences could be demonstrated.

As seen in Table 13.1.1/5, the number of bed-days per thousand persons was slightly higher in IA than in SR for persons under 65 years of age while it was markedly higher in SR than in IA for those 65 years of age or older. Males had much more bed disability in SR than IA while for women the rates are more similar. When the groups are combined, there is a greater number of bed-days in SR than IA. Data from the unexposed control area in urban Toronto (TC) and from the Canada Health Survey are included in the table. The bed disability experience for the Index Area is somewhat lower than Canada as a whole, somewhat higher than the Prairies in general, and

TABLE 13.1.1/3

PERCENTAGE OF ADULTS FREE OF MAJOR ACTIVITY LOSS* IN THE LAST TWO WEEKS
(15 Years and Over)

	AREA			
	IA	SR	DCCI	SR-M
N	1143	355	274	214
% Free of Major Activity Loss	91.4	93.0	97.8	91.6

* For those whose activity status was school, housework, or working outside of the home.

Question 13: DURING THE PAST 2 WEEKS, DID YOUR HEALTH KEEP YOU FROM ________________ (ACTIVITY STATUS) AT ALL?

TABLE 13.1.1/4

PROPORTION OF DAYS FREE OF MAJOR ACTIVITY LOSS* IN THE LAST TWO WEEKS
(15 Years and Over)

	AREA			
	IA	SR	DCCI	SR-M
N	1145	355	276	214
% of Days Free of Any Major Activity Loss	98.4	99.1	99.8	98.3

---

* For those people whose activity status was school, housework, or working outside of the home.

Question 13: DURING THE PAST 2 WEEKS, DID YOUR HEALTH KEEP YOU FROM ____________________ (ACTIVITY STATUS) AT ALL?

TABLE 13.1.1/5

TWO WEEK BED DISABILITY
(MEAN NUMBER OF DAYS PER 1,000 PERSONS)
(15 Years and Over)

	AREA						
	IA	SR	DCCI	SR-M	TC	(CHS)* CANADA	(CHS)* PRAIRIES
N	1386	482	366	287	261	2433	335
15 - 64 years	166	150	110	106		164	94
65+ years	109	773	121	272		548	375
Male	68	132	69	91		139	55
Female	252	293	152	150		281	215
Combined	**158**	**207**	**112**	**118**	**309**	**212**	**137**

* From average number of bed days per person for two week period in July 1978.

Question 12A: HOW MANY DAYS DID YOU STAY IN BED FOR ALL OR MOST OF THE DAY, INCLUDING ANY NIGHTS SPENT AS A PATIENT IN HOSPITAL (IN THE LAST 2 WEEKS)?

appreciably lower than for an unexposed area of Toronto.

13.2 Utilization of Health Services

13.2.1 Orientation

A useful proxy for the health status of a defined population is the use it makes of health professionals and health facilities. These findings must be interpreted with a great deal of caution, however, because (as mentioned in Section 13.0) they are very sensitive to the availability and the access of the facilities and the health professionals. Nevertheless, their frequent use in interprovincial and international comparisons in a standardized manner serves as a useful but subordinate indicator of the level of health of the people of the Index Area, the main comparison area (SR) and the residents of the areas chosen for ancillary comparisons.

Table 13.2.1/1 presents the percentage of persons spending at least one night in any health care facility during the preceding 12 months. IA men were somewhat more likely to have spent a night in hospital than men from the SR. All areas in Alberta show appreciably higher use of institutional health care facilities than urban Toronto (TC) or Canada as a whole.

TABLE 13.2.1/1

PERCENTAGE OF ADULTS SPENDING AT LEAST ONE NIGHT IN ANY HEALTH CARE FACILITY* IN THE LAST TWELVE MONTHS
(15 Years and Over)

	AREA					
	IA	SR	DCCI	SR-M	TC	CHS**
N	1387	484	366	289	261	17492
15-64 years	18.8	16.6	13.0	14.2		9.8
65+ years	24.8	25.0	29.3	22.7		18.3
Male	16.2	11.2	12.6	9.0		7.7
Female	23.3	24.4	18.3	21.8		13.8
Combined	**19.7**	**17.4**	**15.6**	**14.9**	6.5	10.8

* Participants in the MDR study reported nights in a hospital only; no one spent time in a nursing home or convalescent home in the last 12 months.

** Respondents by hospital stay in at least 12 months.

Question 15: IN THE PAST 12 MONTHS, WERE YOU A PATIENT IN A HOSPITAL, A NURSING HOME OR A CONVALESCENT HOME?

In Table 13.2.1/2, we present the percentage of adults who have had an encounter with a health professional in the last two weeks. This proportion refers only to those participants who reported a medical problem. Thus this item excludes most contacts for such purposes as immunization or periodic medical examination of well persons. This question was asked in exactly the same way as in the Canada Health Survey. The results for all areas are similar and somewhat lower than for Canada as a whole, as reported by the Canada Health Survey.

In Table 13.2.1/3 we show the percentage of respondents who used one or more medications in the preceding two days. For medicine taken on the advice of a medical doctor, the percentages for IA and SR are almost identical. In contrast, for medicines taken without the advice of a medical doctor, the proportion is 6.4% greater in the Index Area. Considering all medications, whether prescribed or not, there are no important differences. In each of the four Alberta areas the percentage of respondents using one or more drugs in the last two days is appreciably higher than for either Canada as a whole or an unexposed area of Toronto that served as a control for the Junction Triangle study. The average number of medications taken per person in the preceding two days was 1.2 per person in the IA and 1.1 in the SR. When asked the question in an identical manner Canadians in general reported using 0.8 medications per day and urban Toronto

TABLE 13.2.1/2

PERCENTAGE OF ADULTS WHO HAVE HAD AN ENCOUNTER WITH A HEALTH PROFESSIONAL IN THE LAST TWO WEEKS*
(15 Years and Over)

	AREA				
	IA	SR	DCCI	SR-M	CHS
N	1381	478	366	287	17491
%					
Male	12.7	9.0	9.7	7.1	12.5
Female	15.9	18.1	11.5	16.7	18.4
Combined	**14.3**	**13.2**	**10.7**	**11.5**	**15.5**

* In which a health problem was reported.

Question 3: DID YOU SEE OR TALK TO A HEALTH PROFESSIONAL ABOUT: ______________________ (HEALTH PROBLEM(S) REPORTED FROM THE LAST TWO WEEKS)?

TABLE 13.2.1/3

PERCENTAGE OF RESPONDENTS WHO USED ONE OR MORE MEDICATIONS IN THE PRECEDING TWO DAYS
(15 Years and Over)

	AREA					
	IA	SR	DCCI	SR-M	TC	CHS*
N	1390	485	366	290	260	17492
% on advice of a medical doctor						
Male	29.6	28.2	21.7	23.7		22.4
Female	46.3	48.2	47.6	49.3		38.7
Combined	**37.8**	**37.5**	**35.3**	**35.5**	**33.7**	**30.7**
% without advice of a medical doctor						
Male	39.6	36.7	34.3	34.6		22.7
Female	47.7	37.6	49.2	34.3		30.0
Combined	**43.5**	**37.1**	**42.1**	**34.5**	**25.0**	**26.4**
% of any medication						
Male	56.8	55.2	48.6	51.3		39.6
Female	72.9	69.9	74.9	67.2		57.7
Combined	**64.7**	**62.1**	**62.3**	**58.6**	**49.2**	**48.9**

* Drug use in last 2 days by advice.

Question 16: YESTERDAY OR THE DAY BEFORE, DID YOU TAKE OR USE ANY OF THE FOLLOWING: (LIST OF 11 TYPES OF MEDICATIONS)?

residents 1.0.

Table 13.2.1/4 shows a percentage of children who used one or more medications in the preceding two days. There are no important differences between IA and SR in any category. However, unlike the corresponding results for the adults, the rates for children are similar to those of urban Toronto and Canada as a whole. The mean number of medications taken per child per day, in all areas, was about 1/2 medications per day. This is somewhat less than for children in urban Toronto or in Canada as a whole, both of which reported about 2/3 of a medication per day. The actual figure for both IA and SR is 0.6 medications.

TABLE 13.2.1/4

PERCENTAGE OF CHILDREN WHO USED ONE OR MORE MEDICATIONS IN THE PRECEDING TWO DAYS
(Children ≤ 14 Years)

	AREA					
	IA	SR	DCCI	SR-M	TC	CHS*
N	762	343	265	170	108	5531
% on advice of a medical doctor						
Male	20.1	15.5	16.8	11.5		21.5
Female	17.9	18.7	18.6	14.5		22.3
Combined	**19.0**	**17.2**	**17.7**	**12.9**	**21.3**	**21.9**
% without advice of a medical doctor						
Male	29.7	25.5	34.4	26.4		28.5
Female	26.9	33.5	44.0	32.5		28.4
Combined	**28.4**	**29.7**	**39.3**	**29.4**	**33.3**	**28.4**
% of any medication						
Male	42.1	34.8	44.3	33.3		44.4
Female	39.7	44.5	53.7	41.0		45.3
Combined	**40.9**	**39.9**	**49.1**	**37.1**	**46.3**	**44.8**

* Drug use in last 2 days by advice.

Question 15 (0-1): YESTERDAY OR THE DAY BEFORE, DID THIS CHILD
Question 21 (1-5): TAKE OR USE ANY OF THE FOLLOWING: (LIST OF
Question 40 (5-14): 11 TYPES OF MEDICATIONS)?

13.3 Prevalence of Major Chronic Irreversible Illness

As shown in Table 13.3/1, there are no clinically significant differences in the prevalences of self-reported irreversible illnesses between the residents of IA and SR, or between DCCI and SR-M. All Alberta areas we studied have rates somewhat lower than the urban Toronto area. The prevalences of diabetes and heart disease are similar to those of all of Canada as reported by the Canada Health Survey. The Alberta rates were also similar to the Toronto rates.

Table 13.3/2, shows the prevalence of musculoskeletal ailments for adults. There are higher rates for IA compared to SR and also for DCCI compared to SR-M for "trouble with limbs and/or other bones or joints". In contrast, there were no important differences in responses about "trouble with the back or spine" across the 4 areas.

TABLE 13.3/1

PREVALENCE OF SELF-REPORTED CHRONIC IRREVERSIBLE ILLNESSES
(15 Years and Over)

	AREA				
	IA	SR	DCCI	SR-M	TC
N	1388	485	366	290	260
Problems with eyesight not corrected by glasses	15.4	10.5	11.2	9.3	8.1
Diabetes	2.7	1.4	1.9	1.7	3.3
Epilepsy	0.3	0.4	0.8	0.3	N/A
Heart disease	3.9	4.5	3.0	4.5	5.8
Kidney disease	1.5	1.0	0.3	0.7	1.5

N/A = Not Available

Question 20: DO YOU PRESENTLY HAVE (ILLNESS NAMED)?

TABLE 13.3/2

PREVALENCE OF MUSCULO-SKELETAL AILMENTS
ADULTS
(15 Years and Over)

	AREA			
	IA	SR	DCCI	SR-M
N	1387	485	366	290
% Responding "yes" to any of the following:				
- Trouble with the* back or spine	41.0	38.0	37.4	38.6
- Trouble with the** limbs and/or other bones or joints	52.3	42.3	47.5	40.3

* Yes response to 20(13).
** Yes response to any of 20(14), (15), or (16).

Question 20: DO YOU PRESENTLY HAVE:
13) TROUBLE WITH THE BACK OR SPINE?
14) TROUBLE WITH THE LEGS OR HIPS?
15) TROUBLE WITH THE ARMS OR SHOULDERS?
16) TROUBLE WITH ANY OTHER BONES OR JOINTS?

13.4 Clinical Findings

In this part of the Chapter, we describe clinical findings elicited by questionnaire and physical examination incorporating data from university specialist consultations and corroborating laboratory investigation. We begin with population estimates of general morbidity followed by reports of the rates of the cardinal outcomes. Included under additional health status indicators are self-reported assessments of mental status and measured visual acuity.

13.4.1 General Morbidity

13.4.1.1 Prevalence of Health Problems

In Table 13.4.1.1/1 we show two-week prevalences of any health problem reported spontaneously by the participants. For adults, higher prevalence for IA was explained entirely by the higher prevalence among males. In contrast, the slightly higher prevalence of SR-M compared to DCCI is explained almost entirely by the women. The rates for men and women combined are similar across the four areas, and differences are not clinically significant.

For children there is no clearcut pattern; rates are similar and no differences attain clinical significance. The rates for men and women combined in all the Alberta areas are lower than for the Toronto Junction Triangle sample and appreciably lower in

TABLE 13.4.1.1/1

TWO WEEK PERIOD PREVALENCE OF ANY REPORTED HEALTH PROBLEMS
%

	AREA				
	IA	SR	DCCI	SR-M	TC*
Adults (15+) N	1377	484	363	290	261
Male	27.0	19.8	19.8	18.6	
Female	33.4	33.6	25.1	32.1	
Combined	**30.1**	**26.2**	**22.6**	**24.8**	**33.7**
Children (5-14) N	523	228	156	141	108
Male	11.8	14.0	10.1	15.3	
Female	14.7	9.1	5.2	7.3	
Combined	**13.2**	**11.4**	**7.7**	**11.4**	**28.7**

* From Toronto Junction Triangle Study unexposed control area.

Question 2 (Adult):	DURING THE LAST TWO WEEKS, HAVE YOU HAD ANY HEALTH PROBLEMS?
Question 4 (5-14):	IN THE PAST TWO WEEKS, HAS THIS CHILD'S HEALTH LIMITED THE KIND OR AMOUNT OF VIGOROUS ACTIVITIES HE OR SHE CAN DO, SUCH AS RUNNING, LIFTING HEAVY OBJECTS OR TAKING PART IN STRENUOUS SPORTS?

children than in that urban area.

13.4.1.2 Paraclinical (Laboratory) Findings

Participants at least 7 years of age were tested for visual acuity by using a 20 foot distance standard eye chart. For each eye, acuity was read from the line above the line in which two or more errors were made. As shown in Table 13.4.1.2/1, approximately 9% of all participants had visual impairment as defined by visual acuity of 20/40 or poorer in both eyes. The difference in prevalence between IA and SR was less than 1%.

Participants at least 7 years of age had a random midstream urinalysis performed using a reagent strip. Women menstruating at the time of examination were excluded (N = 36). As shown in Table 13.4.1.2/2, the percentages of participants with specific urine abnormalities were similar among all areas. The largest differences were as follows: IA had a 1% greater proportion with proteinuria and glycosuria than did SR. DCCI had a 1.3% higher rate of hematuria than SR-M. The findings were summarized by measuring the percentage of participants free of all measured urinary abnormalities. These were as follows: 89.8% for IA, 90.7% for SR, 93.1% for DCCI, and 93.4% for SR-M.

All participants at least 7 years of age had blood samples drawn for biochemical analysis. The proportions of participants with non-fasting biochemical values outside the facility laboratory reference ranges (of the Foothills Hospital) are

TABLE 13.4.1.2/1

PERCENTAGE OF PARTICIPANTS WITH VISUAL IMPAIRMENT BY AREA*
(20/40 or poorer in both eyes)

	AREA			
	IA	SR	DCCI	SR-M
N	1768	649	436	392
Visual Impairment				
Present	9.4	8.5	8.7	8.7

* Subjects who customarily wore glasses were tested with their glasses on.

TABLE 13.4.1.2/2

PERCENTAGE OF PARTICIPANTS WITH SPECIFIC ABNORMALITIES ON URINALYSIS FOR ALL PARTICIPANTS COMBINED AND BY AREA*

Abnormality	All Participants	AREA			
		IA	SR	DCCI	SR-M
N	2759	1674	637	448	391
Protein $\geq$ .3g/L	5.8	6.5	5.5	3.6	4.6
Blood $\geq$ trace	1.8	1.7	2.2	1.8	0.5
Glucose $\geq$ 13.9 mmol/L	0.9	1.3	0.3	0.5	0.5
Bilirubin $\geq$ moderate	0.1	0.1	0.0	0.2	0.0
Urobilinogen $\geq$ 34umol/L	0.1	0.1	0.0	0.5	0.0
Ketones $\geq$ 1.5 mmol/L	0.5	0.5	0.5	0.7	0.3
Percentage of Participants Free of Any Abnormality in Urinalysis		90.4	91.7	93.5	94.1

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* Random midstream urine was tested by a reagant strip. Women menstruating at time of examination were excluded (N = 36).

presented in Table 13.4.1.2/3 and the mean levels for each area are presented in Table 13.4.1.2/4. For all participants combined, the percentage of participants with abnormal values was less than 5% except for serum calcium, inorganic phosphate, cholesterol, alkaline phosphatase, and lactate dehydrogenase. For the first three of these values, reference ranges refer only to fasting serum samples because levels are altered by the recent ingestion of food. The findings were summarized by measuring the percentage of participants free of all measured biochemical abnormalities. These were as follows: 45.4% for IA, 43.4% for SR, 46.4% for DCCI, and 43.8% for SR-M.

An electrocardiogram was performed on participants at least 25 years of age in a non-fasting state. As shown in Table 13.4.1.2/5, the percentages of participants with specific electrocardiographic abnormalities were similar among all areas. The largest difference found was a 4.2% increase in ST-T Wave Abnormalities in SR-M as compared to DCCI. The percentage of participants with any abnormality was slightly lower in IA than in SR, and lower in DCCI than in SR-M.

TABLE 13.4.1.2/3

PERCENTAGE OF PARTICIPANTS WITH SPECIFIC ABNORMALITIES
OF SERUM BIOCHEMISTRY BY AREA*

Abnormality	All Participants	AREA			
		IA	SR	DCCI	SR-M
N	2782	1695	639	448	387
Protein (<60 g/L)	0.7	0.8	0.5	0.7	0.5
Albumin (<30 g/L)	0.0	0.0	0.0	0.0	0.0
Calcium (>2.54 mmol/L)	9.0	9.4	7.4	9.8	6.7
Inorganic Phosphate (>1.5 mmol/L)	11.3	10.6	12.5	12.3	13.4
Cholesterol (>6.5 mmol/L)	13.8	13.5	13.2	15.9	14.5
Urate (males >535 M, females >460 umol/L)	1.3	1.2	1.7	0.7	1.[illegible]
Urea (>9.2 mmol/L)	2.5	3.0	1.4	2.2	1.3
Bilirubin (>20 mmol/L)	2.3	2.6	1.9	1.6	1.9
Alkaline Phosphatase (>115 units/L and age >21 years)	6.8	7.7	5.2	6.0	3.6
Creatine Kinase (>225 units/L)	4.1	4.6	3.1	3.8	2.3
Lactate Dehydrogenase (>200 units/L)	5.1	6.3	3.9	2.0	3.1
Aspartate Aminotranferase (>41 units/L)	1.2	1.0	1.9	1.3	1.8
Percentage of Participants Free of Any Biochemical Abnormality		55.8	56.9	56.7	57.5

* Denominator used was all these with biochemical results available. Fasting was not requested prior to serum sampling. Abnormal levels were defined by a priori laboratory clinical ranges.

TABLE 13.4.1.2/4

MEAN LEVELS OF SERUM BIOCHEMISTRY FOR ALL PARTICIPANTS AND BY AREA*

Biochemical Value	AREA			
	IA	SR	DCCI	SR-M
N	1695	639	448	387
Protein	68.60	68.39	68.05	68.18
(g/L)	(.10)	(.14)	(.19)	(.19)
Albumin	45.83	45.45	45.42	45.47
(g/L)	(.07)	(.10)	(.13)	(.12)
Calcium	2.434	2.436	2.441	2.438
(mmol/L)	(.002)	(.003)	(.005)	(.004)
Inorganic Phosphate	1.186	1.202	1.200	1.211
(mmol/L)	(.005)	(.009)	(.011)	(.012)
Cholesterol	5.18	5.12	5.33	5.15
(mmol/L)	(.03)	(.05)	(.06)	(.06)
Urate	304.	318.	317.	319.
(umol/L)	(2)	(3)	(4)	(4)
Urea	5.40	5.13	5.37	5.11
(mmol/L)	(.04)	(.06)	(.08)	(.07)
Bilirubin	7.61	7.39	7.06	7.46
(umol/L)	(.12)	(.17)	(.18)	(.22)
Alkaline Phosphatase	130.	134.	126.	134.
(units/L)	(2)	(4)	(4)	(5)
Creatine Kinase	92.	80.	78.	76.
(units/L)	(2)	(3)	(4)	(3)
Lactate Dehydrogenase	148.1	140.6	138.7	138.7
(units/L)	(.8)	(1.1)	(1.4)	(1.5)
Aspartate Aminotransferase	18.7	18.5	17.8	18.2
(units/L)	(.4)	(.3)	(.7)	(.4)

* Fasting prior to serum sampling was not requested.

( ) Standard errors.

TABLE 13.4.1.2/5

PERCENTAGE OF PARTICIPANTS AT LEAST 25 YEARS OF AGE WITH SPECIFIC ELECTROCARDIOGRAPHIC ABNORMALITIES FOR ALL PARTICIPANTS COMBINED AND BY AREA*

Abnormality	AREA			
	IA	SR	DCCI	SR-M
N	1115	371	281	222
Any Abnormality	22.1	23.5	22.8	23.0
Ectopy	4.7	5.4	4.3	3.6
Tachycardia Supraventricular	1.2	0.8	0.0	0.5
Ventricular	0.5	0.0	0.0	0.0
Atrio-ventricular Block	2.4	2.2	2.1	3.2
Atrial Enlargement	0.4	0.3	0.7	0.5
Conduction Defects	12.1	11.1	10.0	11.3
Ventricular Hypertrophy	2.2	1.1	1.8	1.4
Infarction	2.3	1.6	1.8	1.4
ST-T Wave Abnormalities	10.1	10.2	7.5	11.7

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* Abnormality defined by an ECG - computer analysis program. [Marquette MUSE (125L)].

13.4.1.3 Rates of Diagnosed Disease

Taking into account all diagnoses written by physicians in judgemental medical examinations, supplemented by information from consultations in the university hospitals, Table 13.4.1.3/1 shows, by rank, the most frequent diagnoses. By far the most common finding was "ostensibly healthy" with the SR showing 5.1% more individuals in that category than IA; SR-M had a 5.4% higher prevalence of such individuals than DCCI.

The results derived from formal clinical algorithms which used data from the questionnaire, and/or ritualized physical examination, and/or laboratory to define specific conditions are presented in Table 13.4.1.3/2. Certainty, expressed as 'possible', 'probable', or 'definite', increased as more disease-related symptoms were present and also if physical signs accompanied symptoms. As described in the Methods Section, the reliability of these diagnoses for comparison purposes was high since the algorithms invoke all clinical and para-clinical data in the same way for all persons regardless of area. Overall, specific conditions had higher prevalences in IA than in SR, and there was a slight trend for DCCI to have higher prevalences than SR-M.

Table 13.4.1.3/3 compares the period prevalence of recorded illnesses in the 1970 cohorts of the four study areas. The Index Area cohort has been modified to include only outmigrants who are first degree relatives of Index Area residents. This was done to make them more similar to the outmigrants tracked in the comparison areas. Table 13.4.1.3/3 shows no important differences between the IA and SR 1970 cohort with respect to heart disease, migraine, epilepsy, chronic lung disease, or diabetes. There is a 7.5% elevation in the period prevalence of hypertension, and a 5.6% elevation in the period prevalance of chronic bronchitis or phlegm lasting more than one year among the IA 1970 cohort as compared to SR.

TABLE 13.4.1.3/1

PERCENTAGE OF ALL PARTICIPANTS WITH MOST COMMON DIAGNOSES MADE BY JUDGEMENTAL AND CONSULTING PHYSICIANS

	AREA			
	IA	SR	DCCI	SR-M
N	2148	821	616	458
Ostensibly healthy	54.0	59.1	50.5	55.9
Uncomplicated hypertension	9.1	7.4	9.3	8.1
Hay fever, allergic rhinitis	8.4	6.9	4.2	8.5
Obesity	5.2	3.7	3.4	3.5
Asthma	3.9	3.4	4.4	2.6
Chronic bronchitis	2.6	3.2	3.6	4.2
Deafness, not otherwise specified	3.1	1.6	1.8	1.8
Osteoarthritis	2.1	1.6	5.0	1.5
Status-post surgery	2.8	2.0	2.1	2.2
Conjunctivitis	2.5	2.1	2.4	2.6

TABLE 13.4.1.3/2

PERCENTAGE OF PARTICIPANTS WITH SPECIFIC CONDITIONS DEFINED BY FORMAL CLINICAL ALGORITHMS: RESULTS ARE PRESENTED BY AREA*

CONDITION		AREA			
		IA	SR	DCCI	SR-M
N		1383	465	348	276
OCULAR					
conjunctivitis	probable	29.4	22.6	23.9	26.1
	definite	1.4	1.5	1.4	1.1
RESPIRATORY					
rhinitis	probable	19.2	13.3	15.2	14.5
	definite	3.2	3.9	2.6	4.7
pharyngitis	probable	21.4	13.8	18.4	17.8
	definite	0.9	3.2	0.9	2.9
chronic bronchitis		12.4	8.6	12.4	9.4
wheezing syndromes	grade 1***	14.2	13.6	16.4	13.8
	grade 2	4.3	2.4	4.6	2.9
	grade 3	2.8	2.4	2.3	2.5
OCULAR AND RESPIRATORY IRRITATION COMBINED**		24.7	20.8	21.0	23.9
CUTANEOUS					
dermatitis	possible	11.5	12.3	14.1	11.6
	probable	2.8	1.5	1.2	2.5
	definite	4.0	2.4	2.3	1.8

* Results based on 2,196 subjects $\geq$ 15 years of age who had a questionnaire, physical examination, and laboratory data available for analysis. The diagnostic algorithms used, due to their length, have been put into Appendix 5.1.6.

** Percentage of participants with at least one of definite conjunctivitis, rhinitis, definite pharyngitis, or chronic bronchitis.

*** Grade of severity of wheezing syndrome.

TABLE 13.4.1.3/2 (CONTINUED)

PERCENTAGE OF PARTICIPANTS WITH SPECIFIC CONDITIONS DEFINED BY FORMAL CLINICAL ALGORITHMS: RESULTS ARE PRESENTED BY AREA*

CONDITION	AREA			
	IA	SR	DCCI	SR-M
N	1379	464	344	275
NEUROLOGICAL				
symptomatic polyneuropathy	0.3	0.2	0.3	0.0
asymptomatic polyneuropathy	0.5	0.0	0.6	0.0
mononeuropathy				
sensory component	1.2	1.1	0.3	0.4
motor component	0.5	0.7	0.6	0.7
essential tremor	0.3	0.2	0.6	0.0
combined neurological***	2.7	1.5	2.0	0.7
OTHER RELATIVELY FREQUENT CONDITIONS				
HYPERTENSION	9.7	7.3	9.2	6.5
complicated****	4.2	1.7	2.9	1.4
OBESITY	37.4	36.3	35.3	33.7
DEAFNESS				
one ear	3.8	5.2	2.3	5.1
both ears	4.5	2.4	3.5	1.8
BACK PAIN				
any back pain	30.7	34.1	33.0	35.5
with any neurological signs	10.3	4.7	6.1	4.4
HEART MURMUR				
systolic only	15.6	12.0	14.9	10.9
diastolic with or without systolic	0.7	0.9	0.0	1.5

*** Percentage of participants with at least one of; motor or sensory neuropathy, symptomatic or assymptomatic polyneuropathy, or essential tremor.

**** Result based on 1739 subjects ≥25 years of age who had a questionnaire, physical examination, laboratory data, and an elective cardiogram available for analysis.

TABLE 13.4.1.3/3

PERIOD PREVALENCE OF REPORTED ILLNESSES 1970 TO 1985
(1970 Cohort)

	AREA			
	IA*	SR	DCCI	SR-M
N	1259	428	338	252
Heart Disease**	11.6	9.4	8.3	8.3
Hypertension** (High Blood Pressure)	18.7	11.2	16.6	11.9
Migraine***	9.9	7.0	6.5	5.2
Epilepsy***	0.6	0.5	1.2	0.0
Chronic Bronchitis or** Phlegm Lasting more than 1 Year	16.4	10.8	12.7	10.7
Chronic Lung Disease** (Emphysema)	1.0	0.0	1.2	0.0
Diabetes***	3.0	1.6	1.8	2.4

* Includes only outmigrants who are first degree relatives.
** Positive answer to the direct question "Were you ever told by a doctor that you had (illness named)".
*** Positive answer to the direct question "Do you presently have (illness named)".

13.4.2 Cardinal Outcomes

13.4.2.1 Cardinal Symptoms, Signs and Diagnoses

In Table 13.4.2.1/1, we show the two-week period prevalence of cardinal symptoms for adults. Most of the symptoms were reported more frequently by residents of the IA than SR. In the comparison of DCCI vs. SR-M the rates are similar between the two areas.

In Table 13.4.2.1/2 as in the previous table, we show the two-week prevalence of symptoms declared in advance as cardinal. These are reports of parents about their children. We have put asterisks for symptoms not elicited among children ages 1-4. Again, several reported symptoms are higher among children in IA than in SR. DCCI and SR-M are more similar, without any trend favouring either group.

In Table 13.4.2.1/3, we show the two-week prevalence of at least one among fifteen probed cardinal symptoms considered important. Prevalences are slightly higher for both adults and children in the IA Area than in SR. Differences between DCCI and SR-M are clinically inconsequential.

Table 13.4.2.1/4 shows no clinically significant differences in any of the contrasts between IA and SR in the percentage of objective cardinal physical signs observed in participants. Neither are there any such differences between the DCCI and the

TABLE 13.4.2.1/1

TWO WEEK PERIOD PREVALENCE OF CARDINAL SYMPTOMS
ADULTS
(15 Years and Over)

	AREA			
	IA	SR	DCCI	SR-M
N	1390	485	366	290
Ocular Symptoms				
Itching, burning or watering of eyes	30.7	24.1	24.9	27.2
Respiratory Symptoms				
Itching, burning or running nose not due to a cold	22.3	16.7	17.5	18.6
Irritation of the throat not due to a cold	22.2	16.5	18.3	20.0
Feeling of suffocation	11.9	8.3	7.7	9.3
Shortness of Breath	23.5	20.2	21.0	20.0
Cough	26.5	25.6	28.8	27.9
Phlegm	26.4	22.1	22.7	19.0
Wheezing	10.6	9.9	10.9	10.0
Cutaneous Symptoms				
Burning or itching of the skin	18.3	15.9	16.9	15.9
Neurological Symptoms				
Weakness of hands, feet, fingers, or toes	8.4	6.2	6.8	7.6
Loss of feeling in the hands, feet, fingers, or toes	9.8	4.5	6.0	5.2
Tingling in the hands, feet, fingers, or toes	17.9	10.9	13.9	8.6
Trembling of the hands	14.0	11.1	12.0	10.7
Gastro-Intestinal Symptoms				
Nausea	16.8	15.5	10.7	14.8
Other Symptoms				
Tiredness or Fatigue	33.8	28.3	30.1	27.9

TABLE 13.4.2.1/2

TWO WEEK PERIOD PREVALENCE OF CARDINAL SYMPTOMS
CHILDREN
(1 - 14 Years)

	AREA			
	IA	SR	DCCI	SR-M
N	726	341	263	170
N	527*	228*	158*	141*
%				
Ocular Symptoms				
Itching, burning or watering of eyes	15.7	10.6	10.7	9.4
Respiratory Symptoms				
Itching, burning or running nose not due to a cold	16.7	11.4	10.3	13.5
Irritation of the throat not due to a cold	12.3	9.1	8.8	9.4
Feeling of suffocation	4.1	2.1	2.7	2.4
Shortness of Breath*	4.6	3.1	3.8	3.6
Cough	11.9	10.3	8.4	8.8
Phlegm	7.3	5.9	3.7	4.9
Wheezing	5.1	3.8	3.8	4.1
Cutaneous Symptoms				
Burning or itching of the skin	11.3	11.7	9.9	11.2
Neurological Symptoms				
Weakness of hands, feet, fingers, or toes*	2.1	1.8	0.6	2.1
Loss of feeling in the hands, feet, fingers, or toes*	0.2	0.4	0.6	0.7
Tingling in the hands, feet, fingers, or toes*	1.5	2.6	0.6	2.8
Trembling of the hands*	2.7	2.2	1.3	2.1
Gastro-Intestinal Symptoms				
Nausea	16.7	16.7	17.9	16.5
Other Symptoms				
Tiredness or Fatigue	14.6	12.9	14.1	12.9

* Not elicited for children ages 1 - 4.

TABLE 13.4.2.1/3

TWO WEEK PERIOD PREVALENCE OF AT LEAST ONE PROBED CARDINAL SYMPTOM (Out of 15)*

	AREA			
	IA	SR	DCCI	SR-M
Adults (15+) N	1392	485	364	290
Male	76.1	70.9	71.3	71.6
Female	83.4	78.0	77.4	78.5
Combined	**79.4**	**74.2**	**74.3**	**74.8**
Children (1-14)** N	726	341	263	170
Male	52.8	47.5	51.5	49.4
Female	48.4	45.3	46.6	42.2
Combined	**50.7**	**46.3**	**49.1**	**45.9**

* See list in previous table.
** Ten symptoms only available for children ages 1-5.

TABLE 13.4.2.1/4

PREVALENCE OF CARDINAL PHYSICAL SIGNS IN PARTICIPANTS

	AREA			
	IA	SR	DCCI	SR-M
N	2151	816	616	454
Percentage with:				
No signs	63.5	54.8	69.6	54.0
One sign	25.6	33.1	23.4	33.5
At least one sign	36.5	45.2	30.4	46.0

SR-M. For this group of variables, whether one considers the proportion of persons without any signs at all or those with at least one sign (the converse) there is a trend for the IA to have fewer signs than the SR. Similarly, those in the exposed DCCI area have fewer signs than those in SR-M.

Table 13.4.2.1/5 shows no important differences between IA and SR in cardinal physical signs frequently observed by physicians in the medical ritualistic examination. Red eyes and red mucosa were observed at lower rates both in IA and DCCI compared to their reference population.

In Table 13.4.2.1/6, we show differences in rates of diagnoses declared cardinal prior to completion of the field work and before the analysis. There are no important differences between IA and SR.

TABLE 13.4.2.1/5

PERCENTAGE OF SPECIFIC SELECTED CARDINAL PHYSICAL SIGNS OBSERVED IN MEDICAL RITUALISTIC EXAMINATION

	AREA			
	IA	SR	DCCI	SR-M
N	2151	816	616	454
Red Eyes	10.7	17.5	8.8	18.7
Red Mucosa	12.8	24.5	10.4	23.6
Wheezing and crackles in lungs	2.8	2.6	1.8	3.1
Skin rash	3.8	2.3	2.1	2.4
Ear drum abnormalities	9.3	7.5	8.0	7.7
Neurological findings	11.9	7.1	7.6	7.3
Tremor	0.6	0.0	0.7	0.0

TABLE 13.4.2.1/6

PERCENTAGE OF MOST FREQUENT CARDINAL DIAGNOSES BY AREA FROM MEDICAL JUDGEMENTALS AND CONSULTATIONS

	AREA			
	IA	SR	DCCI	SR-M
N	2148	821	616	458
Hay fever, allergic rhinitis	8.4	6.9	4.2	8.5
Asthma	3.9	3.4	4.4	2.6
Chronic bronchitis	2.6	3.2	3.6	4.2
Conjunctivitis	2.5	2.1	2.4	2.6
Dermatitis Not Otherwise Specified	2.7	0.6	2.8	0.7
Peripheral neuropathy and cerebral palsy	2.0	2.6	1.6	1.8
Other diseases of the eye	2.1	1.0	2.4	1.5
Upper Respiratory Tract Infection	1.5	2.0	2.6	1.5
Other diseases of the skin	0.9	0.9	2.4	0.7
Acne	0.9	1.2	1.5	2.2
Congenital anomalies	1.6	1.7	1.0	2.2
Allergic reactions	1.1	0.4	1.1	0.4
Sinusitis acute & chronic	1.0	0.4	0.0	0.7
Urticaria	0.8	0.0	0.3	0.0
Abnormal urine test	0.7	0.7	0.0	0.7
Dyspnea	0.5	0.4	0.7	0.2
Psoriasis	0.5	0.4	0.5	0.4
Emphysema, Chronic Obstructive Pulmonary Disease	0.6	0.1	0.2	0.0
Benign neoplasm of skin	0.2	0.0	1.3	0.0

13.4.3 Additional Health Status Indicators

13.4.3.1 Mental Health Status

Mental status was assessed only with one questionnaire should it have been needed as an explanatory or an adjusting variable. As seen in Table 13.4.3.1/1 when scoring symptoms related to mental health status in the standard way which would categorize perfect health at 0 and clear-cut mental health deficit at scores approaching 70, we find that using a "screening" data-gathering instrument residents in all areas are very near the maximum attainable level of healthy mental status.

TABLE 13.4.3.1/1

MENTAL HEALTH STATUS SCORE*
SYMPTOMATOLOGY
(Range from 0 - 66.9)

	AREA			
	IA	SR	DCCI	SR-M
N	1427	507	370	301
Median Score:				
Male	6.0	4.0	4.0	4.0
Female	9.0	7.0	7.0	7.0
Combined	**7.0**	**6.0**	**6.0**	**6.0**

NOTE: Low scores like these indicate good mental health status.

* From Ilfeld mental health score distribution for Verdun, Quebec 1981-82.

13.4.3.2 Perception of Community Health Hazards

We asked participants if there was anything in the community where they lived which they felt or perceived would affect their health in any way (Table 13.4.3.2/1). Although technically the percentage answering "yes" in IA area is not clinically significant compared to SR, we prefer to judge it of practical significance because the rate one third higher. The question was phrased in order not to be "leading" and some of those responding "yes" in IA could have felt that there were factors in the area affecting their health in a beneficial way. However, that is very unlikely given the known general concerns in the community. In DCCI the percentage of those responding "yes" is exactly the same as in the unexposed SR-M even though the exposure of DCCI participants is very similar to that in IA.

TABLE 13.4.3.2/1

PERCEPTION OF PARTICIPANTS REGARDING FACTORS IN THE COMMUNITY WHICH MAY AFFECT THEIR HEALTH
(15 Years and Over)

	AREA			
	IA	SR	DCCI	SR-M
N	1269	473	362	285
% answering "yes"	20.1	13.5	13.3	13.3

Question 80 (c): IS THERE ANYTHING IN THE COMMUNITY WHERE YOU LIVE THAT AFFECTS YOUR HEALTH IN ANY WAY?

14. SPECIAL STUDIES IN HEALTH STATUS EVALUATION

Certain special studies were needed to address specific concerns of the Index Area Community Advisory Board and the general population of Southern Alberta.

One special study was the measurement of selected trace metal concentrations in participants. This was done predominantly by using hair samples; blood samples were used for mercury measurements and to confirm abnormal trace metal results found in hair. The results are presented in section 14.1.

Hutterites were excluded from the summer health status evaluation because their lifestyle, certain distinct biological characteristics, and unique sociodemographic profiles would have made it difficult to interpret findings in data gathered from them. Nevertheless, it was possible to identify and compare trace metal concentrations between one Index Area colony and one Stirling-Raymond area colony. The Community Advisory Board pointed out to us that the Hutterite community consumed food mostly grown within the area, and could thus be a sensitive indicator of local and environmental factors that might mediate tissue levels of trace metals. Accordingly, the second special study was measurement of trace metals in hair and blood in two Hutterite colonies. The results are presented in section 14.2.

Because airborne pollution can affect respiratory health, physiologic measures of respiratory function were deemed important and were designated cardinal variables. The results from the special study on respiratory function are presented in section 14.3.

Finally, the Community Advisory Board members expressed their perception that in the Index Area, certain symptoms and signs were worse during the winter than the summer. In effect, they were concerned that we may have come to do clinical measurements in the least appropriate season of the year. In response to this concern, we re-examined randomly selected subsamples of the IA and SR groups during the last two weeks in January to determine changes in respiratory function and cardinal findings most vulnerable to seasonal variation. The health experience of the subsample in the preceding six months was also assessed. The results of this Winter Reassessment are given in section 14.4.

14.1 Trace Metal Study

Hair samples for trace metal analyses were obtained from participants with an adequate amount of hair, and blood samples for mercury obtained from those at least 7 years of age. Distributions for each trace metal were expressed by percentiles as shown in Table 14.1/1. For all participants combined, the lower fifth percentile value was at or below the lower limit of laboratory detection for all trace metals. The upper ninety-fifth percentile for all trace metal values was not considered to be high by either the Quebec or Mayo Clinic Laboratories. Median values in general were close to the lower limit of detection and were similar among areas. An exception was IA hair cadmium, median value of 0.13, which was lower than for the other three areas.

Table 14.1/2 presents trace metal values categorized according to an a priori laboratory classification which is described in detail in Table 14.1/3. For all participants combined, more than 94% of values were either within the undetectable (UD) or normal (NN) range. IA had an equal or lower percentage of people than SR with high (HH) results than SR for each of the trace metals examined. This relationship continued to hold if those with borderline (NH) were combined with HH results, with the exception of blood mercury. DCCI as compared to SR-M had an equal or lower proportion of people with HH results for each trace metal determination and this relationship persisted when NH and HH results were combined, with the exception of hair arsenic.

Supplementary Note:

It is important to note that hair is a useful "screening" tool for the metals we measured because it is highly sensitive. However, the rate of "falsely elevated" results may be high because hair is easily contaminated from sweat, dust, or dirt. Therefore, for any individual, a high value can not be interpreted to mean an increased body burden of the metal in question.

Apart from research purposes, and out of concern for the participants, those with results in the HH range were notified and a blood sample (urine sample for arsenic) was obtained to determine whether or not the hair had been contaminated. This follow-up is described in appendix 14.1.

TABLE 14.1/1

TRACE METAL VALUES FOR ALL PARTICIPANTS COMBINED AND BY AREA DISTRIBUTIONS ARE EXPRESSED BY PERCENTILES.

TRACE METAL	AREA	NUMBER	PERCENTILES				
			Median	95th	75th	25th	5th
	Combined	2835	1.8	3.4	2.3	1.4	1.0*
Mercury	IA	1746	1.8	3.5	2.4	1.5	1.0
(blood)	SR	637	1.8	3.6	2.3	1.4	1.1
ug/L	DCCI	452	1.8	3.2	2.1	1.4	1.1
	SR-M	387	1.8	3.6	2.3	1.4	1.1
	Combined	3302	0.3	1.0	0.5	0.2	0.1*
Mercury	IA	1967	0.3	0.9	0.5	0.3	0.1
(hair)	SR	760	0.3	1.1	0.5	0.2	0.2
ug/gm	DCCI	575	0.4	1.1	0.5	0.3	0.2
	SR-M	428	0.4	1.1	0.5	0.2	0.2
	Combined	3302	0.05	0.12	0.05	0.05	0.05*
Arsenic	IA	1967	0.05	0.12	0.05	0.05	0.05
(hair)	SR	760	0.05	0.13	0.05	0.05	0.05
ug/gm	DCCI	575	0.05	0.14	0.06	0.05	0.05
	SR-M	428	0.05	0.15	0.05	0.05	0.05
	Combined	3302	0.15	1.11	0.33	0.06	0.05*
Cadmium	IA	1967	0.13	0.92	0.27	0.05	0.05
(hair)	SR	760	0.21	1.48	0.46	0.10	0.05
ug/gm	DCCI	575	0.18	1.50	0.40	0.08	0.05
	SR-M	428	0.21	1.65	0.45	0.10	0.05
	Combined	3302	1.5	11.1	3.3	0.7	0.5*
Lead	IA	1967	1.3	9.6	2.8	0.7	0.5
(hair)	SR	760	1.7	12.3	3.9	0.9	0.5
ug/gm	DCCI	575	1.6	12.8	3.8	0.8	0.5
	SR-M	428	1.7	13.9	3.7	0.9	0.5
	Combined	3302	0.4	0.7	0.5	0.3	0.1*
Selenium	IA	1967	0.3	0.7	0.4	0.3	0.1
(hair)	SR	760	0.4	0.8	0.5	0.3	0.2
ug/gm	DCCI	575	0.4	0.7	0.5	0.3	0.2
	SR-M	428	0.4	0.8	0.5	0.3	0.2

* Concentration is less than or at the lowest limit of detection for the Centre de toxicologie du Quebec.

TABLE 14.1/2

TRACE METAL VALUES FOR ALL PARTICIPANTS COMBINED AND BY AREA RESULTS ARE EXPRESSED AS THE PERCENTAGE OF PARTICIPANTS WITH VALUES IN EACH OF FOUR CATEGORIES DEFINED ACCORDING TO AN A PRIORI LABORATORY CLASSIFICATION*

Trace Metal	Area	Number	Laboratory Classification			
			UD	NN	NH	HH
Mercury (blood) ug/L	Combined	2835	5.7	93.8	0.5	0.0
	IA	1746	7.4	92.0	0.6	0.0
	SR	637	2.7	96.9	0.5	0.0
	DCCI	452	3.5	96.5	0.0	0.0
	SR-M	387	2.6	96.6	0.8	0.0
Mercury (hair) ug/gm	Combined	3302	8.2	87.7	3.7	0.4
	IA	1967	10.9	85.7	3.0	0.4
	SR	760	4.3	90.5	4.7	0.4
	DCCI	575	4.0	91.0	4.9	0.2
	SR-M	428	4.4	90.0	5.4	0.2
Arsenic (hair) ug/gm	Combined	3302	78.6	21.2	0.1	0.0
	IA	1967	80.3	19.6	0.1	0.0
	SR	760	78.3	21.6	0.0	0.1
	DCCI	575	73.4	26.3	0.4	0.0
	SR-M	428	78.5	21.3	0.0	0.2
Cadmium (hair) ug/gm	Combined	3302	22.7	77.1	0.0	0.2
	IA	1967	27.9	72.1	0.0	0.1
	SR	760	13.7	86.1	0.0	0.3
	DCCI	575	17.2	82.4	0.0	0.4
	SR-M	428	13.8	85.8	0.0	0.5
Lead (hair) ug/gm	Combined	3302	15.4	78.9	4.6	1.1
	IA	1967	17.5	77.8	3.7	1.0
	SR	760	12.1	80.7	5.5	1.7
	DCCI	575	12.2	80.4	6.6	0.9
	SR-M	428	12.4	79.0	6.5	2.1
Selenium (hair) ug/gm	Combined	3302	6.6	89.9	0.0	3.5
	IA	1967	8.3	88.2	0.0	3.5
	SR	760	4.9	91.6	0.0	3.6
	DCCI	575	3.1	93.4	0.0	3.5
	SR-M	428	2.8	93.7	0.0	3.5

* For trace metal values associated with laboratory ranges see Table 14.1/3

UD = Concentration is undetectably low

NN = Concentration within expected range according to both the Quebec Centre de Toxicologie and the Mayo Clinic.

NH = Concentration within expected range for one laboratory and higher than the expected range for the other laboratory. For hair and blood Mercury, NH designates values that lie between expected and high for both laboratories.

HH = Concentration higher than the expected range according to both laboratories.

TABLE 14.1/3

DEFINITION OF A PRIORI LABORATORY CATEGORIES FOR TRACE METAL RESULTS

	Centre De Toxicologie du Quebec			Mayo Clinic, Minnesota
	LOWER DETECTION LIMIT	NORMAL	HIGH*	HIGH*
Hair (ug/gm)				
Arsenic	≃ 0.05	0.1	>1	>10
Cadmium	≃ 0.05	0.4	>5	not defined
Mercury	≃ 0.1	<1.0	>5	>5
Lead	≃ 0.5	5.0	>10	>25
Selenium	≃ 0.1	0.3	>1	not defined
Blood (ug/L)				
Mercury	≃ 1.0	<5.00	>20	>50

* High = Elevated trace metal concentration that may or may not be of clinical importance. Definition of 'high' may vary between laboratories according to whether it signified being only outside normal range or also associated with health problems.

14.2 Trace Metal Study of Hutterites

Among Hutterites, blood mercury, hair arsenic, and hair cadmium values were all within the normal range as shown in Table 14.2/1. The Index Area Hutterites (HUT-IA) as compared to the Stirling/Raymond Area Hutterites (HUT-SR) had slightly greater levels of hair lead and selenium. For all trace metals, HUT-IA as compared to IA had similar proportions within each category of NH and HH except for the HH category of hair selenium, which was approximately 9% higher in HUT-IA than in IA. For all trace metals, HUT-SR and SR had similar proportions within each category of NH and HH except for the NH category of hair lead which was approximately 4% lower in HUT-SR than SR.

TABLE 14.2/1

TRACE METAL RESULTS FOR TWO HUTTERITE COLONIES AND COMPARISON OF RESULTS BETWEEN HUTTERITES AND NON-HUTTERITE STUDY PARTICIPANTS RESULTS ARE EXPRESSED AS THE PERCENTAGE OF PARTICIPANTS WITH VALUES IN EACH OF FOUR CATEGORIES DEFINED ACCORDING TO AN A PRIORI LABORATORY CLASSIFICATION*

Trace Metal	Colony	Number	Laboratory Classification			
			UD	NN	NH	HH
Mercury	IA	1746	07.4	92.0	0.6	0.0
(blood)	HUT-IA	72	15.3	84.7	0.0	0.0
ug/L	SR	637	02.7	96.9	0.5	0.0
	HUT-SR	56	16.1	83.9	0.0	0.0
Mercury	IA	1967	10.9	85.7	3.0	0.4
(hair)	HUT-IA	82	6.1	90.2	3.7	0.0
ug/gm	SR	760	4.3	90.5	4.7	0.4
	HUT-SR	58	0.0	94.8	5.2	0.0
Arsenic	IA	1967	80.3	19.6	0.1	0.0
(hair)	HUT-IA	82	59.8	40.2	0.0	0.0
ug/gm	SR	760	78.3	21.6	0.0	0.1
	HUT-SR	58	74.1	25.9	0.0	0.0
Cadmium	IA	1967	27.9	72.1	0.0	0.1
(hair)	HUT-IA	82	15.9	84.2	0.0	0.0
ug/gm	SR	760	13.7	86.1	0.0	0.3
	HUT-SR	58	22.4	77.6	0.0	0.0
Lead	IA	1967	17.5	77.8	3.7	1.0
(hair)	HUT-IA	82	32.9	62.2	3.7	1.2
ug/gm	SR	760	12.1	80.7	5.5	1.7
	HUT-SR	58	24.1	74.1	1.7	0.0
Selenium	IA	1967	8.3	88.2	0.0	3.5
(hair)	HUT-IA	82	0.0	87.8	0.0	12.2
ug/gm	SR	760	4.9	91.6	0.0	3.6
	HUT-SR	58	1.7	94.8	0.0	3.5

* For trace metal values associated with the above laboratory ranges see Table 14.1/3.

Definition of Abbreviations For Table 14.2/1

HUT-IA - Waterton Colony composed of approximately 95 people living within a few miles east of the Gulf Natural Gas Plan. Results were based on 82 hair and 72 blood samples.

HUT-SR - Cameron Farm Colony composed of approximately 93 people living approximately 30 miles southeast of Lethbridge, Alberta. Results were based on 58 hair and 56 blood samples.

UD = Concentration is undetectably low.

NN = Concentration within expected range according to both the Quebec Centre de Toxicologie and the Minnesota Mayo Clinic.

NH = Concentration within expected range for one laboratory and higher than the expected range for the other laboratory. For hair and blood Mercury, NH designates values which lie between expected and high for both laboratories.

HH = Concentration higher than the expected range according to both laboratories.

14.3 Summary of Spirometric Results Obtained During Health Status Evaluation of Respiratory System

Due to the large amount of information which must be conveyed in this text, only the primary outcome variable for respiratory function, the one-second forced expired volume (FEV_1), is presented in this section. The forced vital capacity (FVC), the mid-maximal expiratory flow (MMEF), the FEV_1/FVC ratio and bronchodilator response are presented in the appendix. The first table in this section describes the participants eligible for spirometry in terms of variables known to influence spirometric results. The second and third tables present unadjusted and adjusted FEV_1 measurements for children and adults. The fourth and fifth tables summarize both the results found in this section and those found in the appendix.

For conceptual purposes and for ease of statistical adjustments, participants were divided into children and adults at the point where the rapid growth phase stops, i.e. where age and height lose their strong correlation. Therefore, unlike age groupings found elsewhere in the study males were divided by age into boys, 7-15 years of age inclusive, and men, at least 16 years of age. Females were divided into girls, 7-13 years of age inclusive, and women, at least 14 years of age.

Table 14.3/1, which compares children by area, shows that IA had the highest ratio of boys to girls. Boys in DCCI tended to be younger and smaller in both height and weight than boys in the other three areas. Girls in IA were slightly younger than in the other three areas. Comparing adults, DCCI had the largest ratio of women to men. Men in IA were older and smoked less than in the other areas. Among women, mean age was greatest in DCCI, and the lowest proportion of current smokers was again found in IA. Of the 2925 participants listed in Table 14.3/1 who came to the study site for spirometry, 2863 had at least one 'acceptable' spirogram (as described by the Epidemiology Standardization Project 1978;118:p 57) available for analysis, and 2710 had a second FEV_1 within 95% of the largest recorded FEV_1. Thus, 98% of these participants had an FEV_1 available for analysis and 95% of these participants had highly reproducible results. In the present study, results were based on the largest 'acceptable' FEV_1.

Table 14.3/2 presents FEV_1 measurements in children by age and sex for each area, unadjusted (crude means) and also adjusted for factors that influence results by two methods: First, values were externally adjusted by expressing them as a percentage of the value predicted using the equations of Knudson et al. (Am Rev Respir Dis 1983;127:725) as reference standards which take into account sex, age, and height. Second, results were 'internally'

TABLE 14.3/1

CHARACTERISTICS OF SUBJECTS BY AREA*

Characteristics by Sex and Age		AREA			
		IA	SR	DCCI	SR-M
Boys N		237	97	62	67
Age		10.8	10.8	10.3	10.9
Height		147	147	144	148
Weight		40	42	38	43
Girls N		160	81	56	49
Age		9.9	10.1	10.3	10.0
Height		143	143	143	144
Weight		37	37	38	38
Men N		687	250	169	150
Age		43.5	40.6	41.8	41.0
Height		177	176	177	176
Smoking:	current	16	22	30	30
	former	24	25	26	32
	never	60	52	45	38
Women N		708	233	185	135
Age		40.5	36.9	43.1	36.4
Height		164	164	163	164
Smoking:	current	14	19	29	28
	former	10	09	18	07
	never	76	72	52	64

* Males were divided by age into boys, 7-15 years of age, and men at least 16 years of age. Females were divided by age into girls, 7-13 years of age, and women at least 14 years of age. Table shows means for age, height and weight. Smallest digit of each mean is of the same magnitude as its standard error. Units of measurement are as follows: age (years), height (centimeters), and weight (kilograms).

TABLE 14.3/2

FEV$_1$ MEASUREMENTS IN CHILDREN BY AREA*

		AREA			
FEV$_1$ by Sex and Age	Number	IA	SR	DCCI	SR-M
Boys N		236	97	57	67
Unadjusted values					
7-9 years	147	1.82	1.64	1.73	1.61
10-11 years	89	2.29	2.14	2.25	2.22
12-13 years	98	2.86	2.98	3.18	3.03
14-15 years	56	3.91	3.85	3.28	4.06
all ages	390	2.52	2.45	2.31	2.52
Girls N		160	81	53	49
Unadjusted values					
7-9 years	115	1.68	1.55	1.62	1.57
10-11 years	100	2.29	2.22	2.17	2.29
12-13 years	79	2.82	2.85	2.67	2.81
all ages	294	2.17	2.13	2.14	2.16
Boys and Girls					
Unadjusted values	684	2.38	2.31	2.23	2.37
		(0.04)	(0.06)	(0.07)	(0.08)
Adjusted (internal)**					
7-9 years	262	2.21	2.06	2.17	2.03
10-11 years	189	2.27	2.18	2.14	2.21
12-13 years	177	2.23	2.26	2.23	2.27
14-15 years	56	2.44	2.30	2.48	2.39
Adjusted (external)***					
% predicted	684	103.4	100.1	101.5	100.6
		(0.6)	(0.9)	(1.1)	(1.1)

* Children were defined as females 7 to 13 years of age and males 7 to 15 years of age, inclusive. Table shows mean (standard error) in litres.

** Age-area specific least squares means taken at the mean value of sex, height, and $\log_e$ (weight).

*** Actual values expressed as a percentage of predicted by equations of Knudson et al. 1983, which take into account sex, age, and height.

adjusted by multivariate regression analysis using loge (FEV_1) as the dependent variable, age, sex, loge (weight), and height as covariates, and area as the independent variable of interest ($R^2=.87$). Because the area x age term was statistically significant ($p<.01$) the data are presented as age-area specific least squares FEV_1 means taken at the mean values of the covariates sex, height, and loge (weight). Evidence for good sensitivity of FEV_1 measurements can be seen in the generally higher unadjusted mean FEV_1 values for boys as compared to girls and older as compared to younger children. Comparing children in IA to those in SR, unadjusted FEV_1 values were greater for three of the four age groups in boys and two of the three age groups in girls. This slight trend for IA to be greater than SR persisted when the unadjusted values for boys and girls were combined and was confirmed both by internal adjustment and external adjustment.

For children in DCCI as compared to SR-M, mean FEV_1 was greater in three of four age groups for boys and one of three age groups for girls. With boys and girls combined, DCCI showed a slightly smaller unadjusted FEV_1 but a slightly greater externally adjusted value than SR-M. In two of four age groups DCCI had a greater internally adjusted mean FEV_1 than SR-M.

Thus, FEV_1 results for children, both unadjusted and adjusted, were similar across all areas, for the most part within one standard error of one another. Because of the large sample sizes, these standard errors are very small. There was a slight trend for the FEV_1 to be higher in IA than SR.

In Table 14.3/3 the results for adults are presented for each area by sex and smoking status. Results are again presented as unadjusted values, externally adjusted values, and internally adjusted values. The equation used to detect an association between area and FEV_1 after internally adjusting for covariates was of the form FEV_1 = sex, age^2, age^2 x $height^2$, sex x $height^2$, current number of cigarettes smoked daily, number of cigarettes smoked over lifetime, and area ($R^2 = 0.76$). Evidence for good sensitivity of FEV_1 measurements can be seen in the greater unadjusted mean FEV_1 for men as compared to women and the lower mean FEV_1 among smokers as compared to non-smokers. For two of three smoking groups in men and two of three smoking groups in women, the unadjusted mean FEV_1 in IA was greater than or equal to that in SR. For men and women combined, the unadjusted values were lower in IA than SR but the internally adjusted values were equal and the externally adjusted values were very close with a slight trend for IA to show smaller values.

For one of three smoking groups among men, the unadjusted mean FEV_1 was greater in DCCI than in SR-M, and among women it

TABLE 14.3/3

FEV$_1$ MEASUREMENTS IN ADULTS BY AREA*

		AREA			
FEV$_1$ by Sex and Smoking Status	Percentage	IA	SR	DCCI	SR-M
Men N		678	245	157	148
Unadjusted values					
Smoking: current	20	3.96	3.82	4.05	3.83
ex	25	3.75	3.74	3.75	3.68
never	56	4.03	4.17	3.95	4.32
all	100%	3.94	4.00	3.93	4.00
Women N		700	230	169	132
Unadjusted values					
Smoking: current	18	2.96	2.96	2.92	3.01
ex	11	3.13	3.05	2.84	3.15
never	71	2.97	3.02	2.87	3.08
all	100%	2.98	3.01	2.87	3.07
Men and Women N		1378	475	326	280
Unadjusted values		3.45 (0.03)	3.52 (0.04)	3.38 (0.06)	3.56 (0.05)
Adjusted (internal)**		3.44 (0.02)	3.44 (0.02)	3.45 (0.03)	3.47 (0.03)
Adjusted (external)*** by smoking status % predicted					
current	18	99.2 (1.0)	98.1 (1.7)	99.5 (1.4)	100.6 (1.7)
ex	18	100.0 (1.2)	101.5 (1.9)	100.5 (2.1)	101.6 (2.5)
never	63 100%	103.6 (0.5)	104.6 (0.8)	103.0 (1.3)	106.8 (1.1)

* Adults were defined as females at least 14 years of age and males at least 16 years of age. Table shows mean (standard error) in litres.

** Area specific least squares FEV$_1$ means taken at the mean values of sex, age^2, age^2 x height^2, sex x height^2, current number of cigarettes smoked daily, number of cigarettes smoked over lifetime.

*** Actual value expresed as a percentage of value predicted by equations of Knudson et al. 1983,which take into account, sex, age, and height.

was consistently lower in DCCI than in SR-M. For men and women combined, the unadjusted results showed the same trend. The internally adjusted and externally adjusted values show the same trend for DCCI to be slightly lower than SR-M.

Summarizing the results of adults, FEV_1 values once adjusted for influencing factors were similar among all four areas. When the results were internally adjusted, IA was equal to SR and DCCI was lower than SR-M by less than one standard error. These trends were consistent with those found by external adjustment. Although unadjusted values showed larger differences between groups, they cannot be relied upon for accurate comparisons because of the many factors, such as age, sex, height, and weight, that influence FEV_1 results.

To bring together results of the detailed analyses of spirometric results found in this section and its appendix, two summary tables are presented.

Table 14.3/4 summarizes spirometric results obtained in children. The internally adjusted mean values are presented by test, area, and age. In general there are no large differences between IA and SR or between DCCI and SR-M. IA shows slightly more favourable results for 3 of the 4 age groups for FEV_1 and in 3 of the 4 age groups for MMEF. FVC and the FEV_1/FVC ratio are

TABLE 14.3/4

SUMMARY OF SPIROMETRIC MEASUREMENTS IN CHILDREN BY TEST, AREA AND AGE

Spirometric Test		Number	AREA			
			IA	SR	DCCI	SR-M
N			236	97	57	67
FEV_1* (L)	7-9 years	262	2.21	2.06	2.17	2.03
	10-11 years	189	2.27	2.18	2.14	2.21
	12-13 years	177	2.23	2.26	2.23	2.27
	14-15 years	56	2.44	2.30	2.48	2.39
MMEF*(L)	7-9 years	262	2.05	1.66	1.91	1.68
	10-11 years	189	2.49	2.29	2.28	2.38
	12-13 years	177	3.02	3.17	3.05	3.15
	14-15 years	56	3.82	3.65	3.45	3.79
FVC*(L)		684	2.62	2.58	2.63	2.60
FEV_1/FVC*			85.9 (0.4)	83.8 (0.5)	84.4 (0.6)	83.8 (0.6)

* After internal adjustment (see Section 14 and its appendix for details).

N.B. FEV_1, MMEF are stratified by age due to presence of significant age*area interaction slightly more favourable in IA than SR. DCCI as compared to SR-M shows slightly more favourable results in 2 of the 4 age groups for FEV_1 and 1 of the 4 age groups for MMEF. FVC and FEV_1/FVC measurements are slightly more favourable toward DCCI than SR-M.

Table 14.3/5 summarizes spirometric results in adults by test and area. Overall, spirometric results are similar among all 4 areas. Specifically, IA has very similar results to SR in FEV_1, MMEF, and FEV_1/FVC. DCCI as compared to SR-M showed a slightly less favourable FEV_1 and MMEF, a slightly more favourable FVC, and a slightly less favourable FEV_1/FVC ratio.

TABLE 14.3/5

SUMMARY OF SPIROMETRIC MEASUREMENTS IN ADULTS BY TEST AND AREA

Spirometric Test	AREA IA	SR	DCCI	SR-M
N	678	245	157	148
FEV_1*(L)	3.44 (0.02)**	3.44 (0.02)	3.45 (0.03)	3.47 (0.03)
MMEF*(L)	3.27 (0.04)	3.27 (0.05)	3.23 (0.06)	3.31 (0.06)
FVC*(L)	4.41 (0.02)	4.39 (0.03)	4.46 (0.03)	4.44 (0.03)
FEV_1/FVC*	78.5 (0.2)	78.4 (0.3)	77.7 (0.4)	78.6 (0.4)

* After internal adjustment (see Section 14 and its appendix for details).

** Standard error of the mean in parentheses.

14.4 Winter Reassessment

The percentage of people who answered 'yes' to the question: "During the last two weeks, have you had any health problems?" is presented in Table 14.4/1. For those participants retested in the winter, the prevalence percentages of health problems are presented for the summer and winter studies followed by the summer/winter difference. The percentage of those in the total summer study group who reported any health problems is presented in parentheses for each of the two areas. The percentage of total summer participants reporting health problems during the summer was similar to the sample selected for winter retesting. From summer to winter in both IA and SR there was an approximate 15% change in the two week period prevalence of reported health problems. These changes were similar in magnitude and direction for both IA and SR.

Probed symptoms, elicited by direct questioning, were related to ocular, respiratory, cutaneous, neurological, and gastrointestinal symptoms, as well as tiredness or fatigue. For each area, the percentage of winter participants reporting at least one symptom during summer testing and winter retesting along with the summer/winter difference is presented in Table 14.4/2. In parentheses is the percentage of the total summer study group who reported at least one symptom. The percentages

TABLE 14.4/1

TWO WEEK PERIOD PREVALENCE PERCENT OF ANY (REPORTED) HEALTH PROBLEMS IN WINTER REASSESSMENT BY PARTICIPANTS AT LEAST 15 YEARS OF AGE

	IA			SR		
N	157			164		
	Summer	Winter	Diff.	Summer	Winter	Diff.
Spontaneously reported health problems*	26.8	43.3	+16.5	26.2	40.9	+14.7
	(29.8)**			(26.2)**		

* Indicated by a positive response to the following question: "DURING THE LAST TWO WEEKS, HAVE YOU HAD ANY HEALTH PROBLEMS?"

** In parentheses are the two week period prevalence percents for total summer study groups from which winter subsamples were drawn. (N for IA = 1392, and SR = 485 in total group).

TABLE 14.4/2

TWO WEEK PERIOD PREVALENCE PERCENT OF AT LEAST ONE PROBED SYMPTOM IN WINTER REASSESSMENT BY PARTICIPANTS AT LEAST 15 YEARS OF AGE

	IA			SR		
N	157			164		
	Summer	Winter	Difference	Summer	Winter	Difference
Percentage with at least one symptom	79.0 (79.7)*	81.5	+2.5	76.2 (74.2)*	74.4	-1.8

* In parentheses are the two week period prevalence percents for total summer study groups from which winter subsamples were drawn. (N for IA = 1392, and SR = 485 in total group).

of summer participants reporting at least one symptom were similar to the sample selected for winter retesting. IA demonstrated a 2.5% increase in probed symptoms while SR demonstrated a 1.8% decrease. The absolute difference in magnitudes of summer/winter differences between areas was 4.3%.

The percentage of people responding 'yes' to a probed question about new health events occurring since the summer study is presented in Table 14.4/3. Seven percent of IA participants and 12% of SR participants reported the occurence of a health event, a difference between the two areas of 5%. Thus SR showed a larger increase in symptoms than IA.

Table 14.4/4 presents the two week period prevalence percent of specific cardinal symptoms, defined as those symptoms that are known to be or could plausibly be related to sour gas and/or other irritant exposure. They include ocular, respiratory tract, skin, neurological, and gastrointestinal symptoms, and also tiredness. The percentages of winter participants reporting cardinal symptoms in the summer and winter study are presented. In parentheses are the percentages of those reporting cardinal symptoms in the total summer group. The winter participants prevalence percentages were similar to the total study group from which they were drawn, differing in all cases by less than 6% and for the most part by less than 2%. In general, fewer

TABLE 14.4/3

PERCENTAGE OF WINTER PARTICIPANTS AT LEAST 15 YEARS OF AGE REPORTING AT LEAST ONE HEALTH EVENT SINCE THE SUMMER

	IA	SR	DIFFERENCE
N	157	164	
Percentage with at least one health event occurring since the summer assessment	7.0	12.2	-5.2

TABLE 14.4/4
TWO WEEK PERIOD PREVALENCE PERCENT OF CARDINAL SYMPTOMS IN WINTER REASSESSMENT BY PARTICIPANTS AT LEAST 15 YEARS OF AGE

	IA			SR		
N	157			164		
	Summer	Winter	Diff.	Summer	Winter	Diff.
Ocular symptoms						
Itching, burning, or watering of eyes	33.1 (30.9)*	25.5	-7.6	29.3 (24.1)*	20.1	-9.2
Respiratory symptoms						
Itching, burning, or running nose not due to cold	21.0 (22.6)	17.2	-3.8	16.5 (16.7)	10.4	-6.1
Irritation of throat not due to cold	21.7 (22.6)	17.2	-4.5	21.4 (16.5)	17.1	-4.3
Feeling of suffocation	12.1 (11.9)	8.9	-3.2	7.9 (8.3)	6.7	-1.2
Shortness of breath	25.5 (23.9)	20.4	-5.1	18.9 (20.4)	14.0	-4.9
Any Cough	27.4 (26.4)	33.1	+5.7	23.2 (25.8)	32.9	+9.7
Any Phlegm	24.2 (26.3)	32.5	+8.3	22.6 (22.1)	34.2	+11.6
Persistent Wheezing**	12.1 (10.6)	10.8	-1.3	7.9 (9.7)	7.3	-0.6
Cutaneous symptoms						
Burning or itching of the skin	19.7 (18.5)	22.3	+2.6	18.9 (15.9)	13.4	-5.5
Neurological symptoms						
Weakness of hands, feet, fingers or toes	8.9 (8.6)	7.7	-1.2	6.1 (6.2)	5.5	-0.6
Loss of feeling in the hands, feet, fingers or toes	9.6 (9.8)	7.0	-2.6	4.9 (4.5)	3.7	-1.2
Tingling in hands, feet, fingers or toes	18.5 (18.1)	21.7	+3.2	9.8 (10.9)	7.9	-1.9
Trembling of hands	16.6 (14.1)	15.9	-0.7	10.4 (11.1)	12.8	+2.4
Gastrointestinal symptoms						
Nausea	19.8 (16.8)	17.2	-2.6	14.0 (13.5)	18.3	+4.3
Other symptoms						
Tiredness or fatigue	33.8 (33.8)	28.0	-5.8	28.7 (28.3)	19.5	-9.2

* Two week period prevalence percent for total summer study groups from which winter subsamples were drawn (N for IA = 1392, and N for SR = 485 in total group)

** Defined by a positive response to question "DOES YOUR CHEST EVER SOUND WHEEZY OR WHISTLING ... MOST DAYS OR NIGHTS?" Unlike the other was not measured.

participants reported symptoms during the winter than during the summer except for an increase in cough and phlegm (IA and SR), skin irritation (IA only), tingling of extremities (IA only), trembling of hands (SR only) and nausea (SR only). Summer/winter differences in the two areas were in general similar both in magnitude and direction.

Cardinal physical signs were defined as those being associated with or plausibly associated with exposure to sour gas and/or other airborn irritants. They include ocular, respiratory, cutaneous, and neurological findings. The percentages of winter participants with cardinal signs in both the summer and winter study are presented in Table 14.4/5. In parentheses are the proportions of participants in the total summer study group with cardinal signs. The Winter Reassessment sample was similar to the total summer group from which it was drawn in the percentages of observed physical signs. Summer/winter differences were small and inconsistent with the following two exceptions: a 9% decrease in participants with red nasal mucosa in SR and a 9.6% decrease in eardrum abnormalities in IA. With respect to red mucosa, the magnitude of the difference between IA and SR summer/winter difference is approximately 10%.

TABLE 14.4/5

PERCENTAGE OF WINTER PARTICIPANTS AT LEAST 15 YEARS OF AGE WITH CARDINAL PHYSICAL SIGNS OBSERVED IN RITUALISTIC MEDICAL EXAMINATION

	IA			SR		
N		157			164	
	Summer	Winter	Diff.	Summer	Winter	Diff.
Red Eyes	19.8 (14.4)*	20.4	+0.6	25.0 (23.6)	22.0	-3.0
Red Mucosa	15.9 (14.8)	17.2	+1.3	26.2 (27.4)	17.1	-9.1
Wheezing or Crackles in Lungs	3.8 (4.3)	3.8	0	3.0 (4.4)	2.4	-0.6
Skin Rash	5.1 (4.3)	8.3	+3.2	2.4 (3.0)	3.7	+1.3
Ear Drum Abnormalities	15.3 (14.4)	5.7	-9.6	14.0 (12.9)	12.2	- 1.8

Definition of Abbreviations for Table 14.4/5:

Red Eyes = Definitely red sclera, conjunctiva, or lid margins bilaterally.

Red Mucosa = Definitely red nose, mouth, or pharynx mucosa.

Wheezing or Crackles in Lungs = Wheezing or crackles definitely heard by auscultation on either the right or left side of the thorax.

Skin Rash = Bilateral, diffuse, red, rash definitely present.

Ear Drum Abnormalities = Bilateral, definite presence of inflammation, bulging, retraction, fluid in middle ear, perforation, scarring, or tympanostomy tubes.

* Percentages for total summer study groups from which winter subsamples were drawn. (N for IA = 1392, and N for SR = 485 in total group)

Table 14.4/6 summarizes the percentages of winter participants with cardinal physical signs during the summer study and during the winter study. Signs were as defined in Table 14.4/5. In parentheses are the percentages of participants in the total summer study group with cardinal signs. The Winter Reassessment samples, were similar to the total summer study groups from which they were drawn in the proportions of participants reporting cardinal signs; the largest difference was a 4.8% greater proportion of the IA winter subsample reporting at least one sign. The data for IA showed a 3.8% increase from summer to winter in the prevalence of at least one reported sign while SR showed a 6.1%. For the report of 3 or more signs, IA reported at 2.6% decrease while SR reported at 0.6% decrease.

Respiratory function differences between July/August 1985 and January 1986 are presented in Table 14.4/7. One of the two technicians employed during the winter was not a member of the study team during the summer. The two, however, tested similar proportions of participants in each area during the winter so that any technician bias should cancel out. Of the 331 participants tested in the Winter Reassessment, one participant tested was not in the study sample and four others did not have at least one acceptable tracing from both summer and winter. For all winter participants combined, respiratory function diminished between summer and winter for FEV_1, FVC and MMEF. For the primary outcome

TABLE 14.4/6

PERCENTAGE OF WINTER PARTICIPANTS AT LEAST 15 YEARS OF AGE WITH CARDINAL PHYSICAL SIGNS
(15 Years and Over)

	IA			SR		
N	157			164		
	Summer	Winter	Diff.	Summer	Winter	Diff.
At least one sign	42.7 (37.9)*	46.5	+3.8	51.2 (50.8)*	45.1	-6.1
Three signs or more	3.2 (2.6)	0.6	-2.6	3.0 (3.8)	2.4	-0.6

* Percentages for total summer study groups from which winter subsamples were drawn. (N for IA = 1392, and N for SR = 485 in total group)

TABLE 14.4/7

RESPIRATORY FUNCTION DIFFERENCES BETWEEN JULY/AUGUST 1985 AND JANUARY 1986. MEAN RESULTS ARE PRESENTED FOR ALL WINTER PARTICIPANTS COMBINED AND BY AREA

	N	Summer	Winter	Summer-Winter Change	
FEV$_1$ (L)				Mean	Percentage
Combined	326	3.49 (.05)*	3.44 (.05)	-.05	-1.5
IA	166	3.44 (.07)	3.38 (.07)	-.06	-1.6
SR	160	3.55 (.06)	3.50 (.06)	-.05	-1.3
MMEF (L/sec)					
Combined	326	3.28 (.07)	3.15 (.07)	-.13	-3.5
IA	166	3.18 (1.34)	3.00 (1.37)	-.18	-5.6
SR	160	3.40 (1.26)	3.31 (1.21)	-.08	-1.4
FVC (L)					
Combined	326	4.45 (.06)	4.42 (.06)	-.04	-0.8
IA	166	4.40 (.09)	4.38 (.09)	-.02	-0.3
SR	160	4.51 (.08)	4.45 (.08)	-.06	-1.3

Definition of Abbreviations:
FEV$_1$ = second forced expiratory volume
FVC = forced vital capacity
MMEF = mid-maximal expiratory flow

* Standard error

variable, FEV_1, the summer/winter differences were comparable between IA and SR. Summer/winter differences in MMEF and FVC were also similar and in the same direction for both IA and SR. Thus the differences between IA and SR found in the summer study persisted during the winter study.

15. CANCER RISKS AND OUTCOMES

15.1 Results of Primary Analyses

15.1.1 Person-Years of Risk

Methods for the study of cancer risks and outcomes have been described in detail in Chapter 6. The *a priori* primary hypothesis test is based on the cancer experience of the *Index Area 1970 cohort*, which was defined as all individuals who resided within the boundaries of the Index Area at any time during the calendar year 1970. The null hypothesis was that standardized incidence ratios of the Index Area 1970 cohort (standardized against the three prespecified reference populations) would be equal to 1.0. Southern Alberta excluding Calgary, Lethbridge, and Medicine Hat comprised Reference Population 1 (RP1); this latter area represents non-metropolitan Southern Alberta. Census Division 6 excluding Calgary comprised Reference Population 2 (RP2) which contains the DCCI control area. Census Division 2 excluding Lethbridge comprised Reference Population 3 (RP3) which contains the SR control area. Chapter 6 includes a description of the methods used to enumerate the Index Area 1970 cohort, to enumerate the incident cancers, and to calculate the standardized incidence ratios. For convenience, we subdivided the Index Area 1970 cohort into 2 subgroups; namely, the Resident Group (RG), which was defined to consist of those members of the Index Area 1970 cohort who were still resident in the Index Area at the time of the comparative health survey, and the Outmigrant Group (OG), which was defined as all individuals in the Index Area 1970 cohort who had migrated out of the area or had died anytime since 1970.

Table 15.1.1/1 presents the Index Area 1970 cohort subdivided by age group in 1970 and sex. As mentioned earlier, the age groups used in Table 15.1.1/1 and henceforth in this analysis are those utilized by the Alberta Cancer Registry and were specified prior to the analysis of the data. As can be seen in Table 15.1.1/1, there were a total of 2,164 members of the Index Area 1970 cohort (1126 male, 1038 female).

Tables 15.1.1/2 and 15.1.1/3 summarize the person-years of risk for the Index Area 1970 cohort males and females respectively. The males experienced a total of 15,585 person-years of risk while the females experienced a total of 14,590 person-years of risk. Thus, a total of 30,175 person-years of risk were experienced by the entire Index Area 1970 cohort.

TABLE 15.1.1/1

THE INDEX AREA 1970 COHORT BY
SEX AND AGE GROUP IN 1970.

	Index Area 1970 Cohort	
Age Group	Male	Female
<20	459	469
20-34	224	182
35-44	117	121
45-54	129	123
55-64	110	80
65-69	34	24
70+	53	39
Total	1126	1038

2164

TABLE 15.1.1/2

PERSON-YEARS OF RISK FOR INDEX AREA 1970 COHORT MALES BY AGE GROUP AND TIME-INTERVAL

Males

Age Group	1970-74	1975-79	1980-84	Total
<20	2028.5	1346.5	699.0	4074.0
20-34	1238.5	1534.0	1646.5	4419.0
35-44	543.5	546.5	652.0	1742.0
45-54	638.0	541.5	506.0	1685.5
55-64	586.0	634.5	584.0	1804.5
65-69	172.0	284.0	357.5	813.5
70+	287.5	345.0	414.0	1046.5
Total	5494.0	5232.0	4859.0	15,585.0

TABLE 15.1.1/3

PERSON-YEARS OF RISK FOR INDEX AREA 1970 COHORT FEMALES BY AGE GROUP AND TIME-INTERVAL

Females

Age Group	1970-74	1975-79	1980-84	Total
<20	2077.0	1333.5	644.5	4055.0
20-34	1021.0	1406.5	1686.0	4113.5
35-44	563.0	483.0	543.0	1589.0
45-54	637.0	629.0	527.5	1793.5
55-64	431.0	526.0	606.0	1563.0
65-69	130.5	209.5	276.0	616.0
70+	221.5	275.5	363.0	860.0
Total	5081.0	4863.0	4646.0	14,590.0

15.1.2 Incidence Rates for Reference Populations

Table 15.1.2/1 presents the cancer incidence rates for males in the three reference populations categorized by age group and by time interval. For brevity and for ease of comparison, we have combined the rates from all three reference populations into one table (Table 15.1.2/1) and these are given for each age group and each time interval. As a summary measure, we have computed age-standardized incidence rates for each of the three time intervals and each of the three reference populations. These are seen in the last three rows of Table 15.1.2/1. Standardization was performed utilizing the 1976 Alberta male population. Consideration of these standardized rates indicates that the cancer incidence is remarkably similar among the three reference populations and cancer incidence rates have risen with time in each of these three populations. The age-standardized rates are provided merely as summary measures; only the age group, sex and time-interval-specific rates were utilized in the estimation of expected cancers.

An analogous set of incidence rates for females in the reference populations is provided in Table 15.1.2/2. As in the case of males, age-standardized rates have been calculated for the three time intervals and for the three reference populations.

TABLE 15.1.2/1

CANCER INCIDENCE RATES* (PER 100,000) FOR MALES BY AGE GROUP, TIME-INTERVAL, FOR THREE REFERENCE POPULATIONS

Age Group		1970-74	1975-79	1980-84
<20	a)	14.31	13.39	12.32
	b)	10.41	12.43	13.79
	c)	9.55	12.91	7.03
20-34		28.23	39.99	45.58
		37.60	26.25	67.26
		22.86	46.09	44.01
35-44		111.00	106.67	106.47
		102.94	112.09	116.50
		103.38	103.90	88.61
45-54		316.38	342.31	310.30
		277.06	305.14	324.61
		287.58	302.04	316.60
55-64		781.21	893.02	1056.69
		763.36	858.45	979.92
		835.98	814.07	1014.35
65-69		1438.71	1779.14	1700.70
		1257.86	1522.73	1732.62
		1703.70	1972.22	1804.88
70+		2256.31	2774.65	3262.74
		2218.62	2921.50	3379.31
		2497.82	3229.63	3412.97
Age Standardized Rates**		250.87	295.66	325.02
		239.39	266.15	334.43
		265.43	312.47	327.59

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* Includes non-melanotic skin cancer; excludes carcinoma-in-situ

** Standardized to 1976 Alberta male population

a) Reference Population 1 - (Non-Metropolitan Southern Alberta)

b) Reference Population 2 - (Contains DCCI)

c) Reference Population 3 - (Contains SR)

TABLE 15.1.2/2

CANCER INCIDENCE RATES* (PER 100,000) FOR FEMALES BY AGE GROUP TIME-INTERVAL, FOR 3 REFERENCE POPULATIONS

Age Group	1970-74	1975-79	1980-84
<20	a) 7.95	14.04	10.93
	b) 6.78	13.46	12.14
	c) 8.11	11.93	7.47
20-34	50.58	58.78	49.85
	60.99	51.41	44.79
	60.68	55.61	47.30
35-44	190.58	183.07	212.03
	190.87	142.41	182.02
	136.17	206.19	219.93
45-54	402.30	409.04	470.70
	394.62	326.38	469.88
	404.40	431.03	435.73
55-64	788.85	781.31	856.05
	699.45	738.04	785.28
	722.06	820.78	894.12
65-69	1063.39	1121.62	1172.32
	904.35	834.36	1148.33
	1088.00	1371.43	915.66
70+	1456.84	1759.12	1967.91
	1390.48	1523.08	2068.97
	1504.59	1723.08	1821.78
Age Standardized Rates**	242.06	263.25	287.07
	229.05	224.95	282.19
	237.16	274.21	270.69

* Includes non-melanotic skin cancer; excludes carcinoma-in-situ

** Standardized to 1976 Alberta Female population

a) Reference Population 1 - (Non-Metropolitan Southern Alberta)
b) Reference Population 2 - (Contains DCCI)
c) Reference Population 3 - (Contains SR)

Here, standardization was performed utilizing the 1976 Alberta female population. Again, the incidence rates were similar among the three reference populations and generally increased with time.

15.1.3 Incident Cancers

A total of 123 incident cancers were identified among the Index Area 1970 cohort during the period 1970-84. A complete categorization of these incident cancers is provided in Table 15.1.3/1.

Among the RG, a total of 35 cancers were identified, 17 occurring among the males and 18 occurring among the females. These 35 incident cancers occurred in 34 members of the RG; there was one individual in the RG with 2 incident cancers. Of the 35 incident cancers, 20 were non-melanotic skin cancers while the remaining 15 were distributed among the various types of malignancies as seen in Table 15.1.3/1. It is noteworthy that only 29 of these 35 cancers were reported by the RG member at the time of his or her visit to the comparative health survey. An additional 6 cancers, not reported by the individual, were identified solely through linkage with the Alberta Cancer Registry. In 5 of 6 of these unreported cancers, the diagnosis was non-melanotic skin cancer; the sixth was a cancer of the

TABLE 15.1.3/1

INCIDENT CANCERS AMONG THE INDEX AREA 1970 COHORT DURING THE PERIOD 1970-84

	Resident Group		Outmigrant Group		Total
TYPE (ICD-9)	Male	Female	Male	Female	
Gastro-intestinal (150.0 - 150.9)	1	2	10	5	18
Breast (174.0 - 175.9)	0	3	0	6	9
Respiratory (160.0 - 165.9)	0	0	4	2	6
Kidney, Bladder, Prostate (185.0 - 189.9)	4	1	17	3	25
Gynecologic (179.0 - 184.9)	0	1	0	4	5
Lip, Oral, Pharynx (140.0 - 149.9)	2	0	3	0	5
Bone, Soft tissue (170.0 - 171.9)	0	0	0	1	1
Lymphoid, Leukemia (200.0 - 208.9)	0	0	0	1	1
Melanoma (172.0 - 172.9)	0	1	0	1	2
Other (190.0 - 199.9)	0	0	3	3	6
Skin (non-melanoma) (173.0 - 173.9)	10	10	17	8	45
TOTAL	17	18	54	34	123

bladder.

A total of 88 incident cancers were identified in the OG, 54 occurring in the males and 34 occurring in the females. These 88 cancers occurred in 75 members of the OG; there were 64 individuals with 1 incident cancer, 10 individuals with 2 incident cancers, and 1 individual with 4 incident cancers. Of the 88 cancers in the OG, a total of 25 were non-melanotic skin cancers while the remaining 63 cancers were distributed among the various other categories as seen in Table 15.1.3/1.

15.1.4 Standardized Incidence Ratio Analyses

Having given all the background data, we are now in position to describe the standardized incidence ratio analysis which represents the primary test of hypothesis in this study. The results of this analysis are presented in Table 15.1.4/1.

Table 15.1.4/1 presents observed and expected numbers of cancers for the Index Area 1970 cohort males and females respectively.

The primary standardized incidence ratio analysis is presented in the bottom panel of Table 15.1.4/1. There were a total of 78 incident cancers in the Index Area 1970 cohort.

TABLE 15.1.4/1

STANDARDIZED INCIDENCE RATIOS (SIR) EXCLUDING NON-MELANOTIC SKIN CANCER FOR THE INDEX AREA 1970 COHORT RELATIVE TO THE THREE REFERENCE POPULATIONS

Population	Observed	Expected*	Expected**	Expected***
Index Area 1970 Cohort Males	45	49.6	49.6	52.7
Index Area 1970 Cohort Females	33	36.3	34.2	35.1
Index Area 1970 Cohort Total	78	85.9	83.8	87.8
SIR* (95% CI)		0.91 (0.67, 1.26)		
SIR** (95% CI)			0.93 (0.68, 1.29)	
SIR*** (95% CI)				0.89 (0.65, 1.23)

* Southern Alberta excl. Calgary, Lethbridge, & Medicine Hat (RP1)
** Census Division 6 excl. Calgary (RP2) - contains DCCI
*** Census Division 2 excl. Lethbridge (RP3) - contains SR

Based on the three reference populations, the expected numbers of cancers were 85.9, 83.8, and 87.8 respectively. These data give rise to standardized incidence ratios of 0.91, 0.93, and 0.89 respectively. The 95% confidence intervals provided for each standardized incidence ratio indicate that they are not statistically significantly different than unity.

The preceding analysis excludes non-melanotic skin cancers in both the observed and expected totals. To test the contribution of these skin cancers on the results, we conducted a second standardized incidence ratio analysis in which non-melanotic skin cancers were included. The results of this latter analysis are presented in Table 15.1.4/2.

There were a total of 123 malignancies including non-melanotic skin cancers observed in the Index Area 1970 cohort (Table 15.1.4/2). Based on the 3 reference populations respectively, there were 117.3, 113.1, and 119.5 such cancers expected in the cohort. These data give rise to standardized incidence ratios of 1.05, 1.09, and 1.03 respectively. Thus, even with the inclusion of non-melanotic skin cancers, in no case is the SIR significantly different from unity.

TABLE 15.1.4/2

STANDARDIZED INCIDENCE RATIOS (SIR) INCLUDING NON-MELANOTIC SKIN CANCER FOR THE INDEX AREA 1970 COHORT RELATIVE TO THE THREE REFERENCE POPULATIONS

Population	Observed	Expected*	Expected**	Expected***
Index Area 1970 Cohort Males	71	69.1	68.2	72.3
Index Area 1970 Cohort Females	52	48.2	44.9	47.2
Index Area 1970 Cohort Total	123	117.3	113.1	119.5
SIR* (95% CI)		1.05 (0.81, 1.36)		
SIR** (95% CI)			1.09 (0.84, 1.41)	
SIR*** (95% CI)				1.03 (0.80, 1.33)

* Southern Alberta excl. Calgary, Lethbridge, & Medicine Hat (RP1)
** Census Division 6 excl. Calgary (RP2) - contains DCCI
*** Census Division 2 excl. Lethbridge (RP3) - contains SR

To summarize the results of the primary analysis, we detected no excess in overall cancer incidence experienced by the Index Area 1970 cohort during the Incidence Period. The data suggest that the overall cancer experience of this cohort during the period 1970-84 is remarkably similar to that which should be expected based on the 3 reference populations, whether non-melanotic skin cancers are included or not.

15.1.5 Post-Hoc Sample Size Considerations

In any investigation where the primary hypothesis test is negative, it is important to consider the possibility of type II error. Sample size requirements were considered prior to the study and the *a priori* considerations may be found in section 6.2.2. These were based on an expectation of 102 incident cancers in the Index Area 1970 cohort.

In fact, the number of expected cancers based on reference rates (approximately 120) is somewhat higher than anticipated so that the study has greater power than expected. This underestimation was due both to our use of crude rates in the *a priori* calculations and to a shift in the person-years of risk toward the older age groups.

Post-hoc power calculations may now be performed. Given 120 expected cancers and given a hypothetical SIR as low as 1.25 with alpha = 0.05, the power is 0.83 and 0.73 for one and two-sided tests respectively. Under the same conditions, the power to detect an SIR of 1.5 with either a one or two-sided test is greater than 0.99. Thus, the probability that we have failed to detect a 25% increase is small, and the possibility that we have missed an increase as large as 50% is extremely remote.

15.2 Results of Secondary Analyses

The previous section (15.1) presented the primary analyses which were pre-specified as the central hypothesis test in this study. We also conducted several analyses to test for the presence of bias, to test the effect of inaccurate information, and to provide ancillary data. In some cases, these analyses were not specified prior to the study as their feasibility was not known until the data collection had been completed. The results of these secondary analyses are described in the sections that follow.

15.2.1 Stratification by Certainty

As noted earlier, a certainty code was assigned to each outmigrant to assess the overall quality of the information regarding that individual. This is described in section 6.1.3.2.

The reader will recall that a certainty code of 1 was assigned to outmigrants whose information was considered certain by virtue of replication from several sources or to outmigrants for whom a mailed questionnaire was returned in the Outmigrant Survey.

To test whether inaccuracy of information might have affected our results, we conducted a second standardized incidence ratio analysis which was restricted only to outmigrants with a certainty code of 1. A total of 970 out of 1,163 outmigrants (83.4%) had certainty codes of 1 and were thus felt to have reliable information. We carried out a second analysis in which the Index Area 1970 cohort was modified to consist of the RG plus only those members of the OG with certainty codes of 1. In this analysis, a total of 91 incident cancers (57 male, 34 female) were observed in the modified Index Area 1970 cohort. Based on expected rates derived from reference population 1 (non-metropolitan Southern Alberta), the number of expected cancers was 99.9 (59.3 male, 40.6 female). These data give rise to a standardized incidence ratio of 0.91 (0.69, 1.23).

We conducted a similar analysis excluding non-melanotic skin cancers. A total of 51 such incident cancers were identified in the modified Index Area 1970 cohort. Again, based on rates from reference population 1 (non-metropolitan Southern Alberta), there were a total of 73.2 expected cancers (42.5 male, 30.7 female).

These data give rise to a standardized incidence ratio of 0.70 (0.48, 0.99). Although this indicates a statistically significant deficit of cancers in the modified Index Area 1970 cohort, this result must be interpreted with caution. First, several analyses have been undertaken so there is the problem of multiple comparisons. Second, our prespecified alternate hypothesis was one-sided in an investigation which sought to determine only whether there was an overall excess of cancers in the Index Area. Third, this result is based on a secondary analysis that was not prespecified to be the central analysis of interest.

The most important conclusion which should be drawn from these results concerning the modified Index Area 1970 cohort is that when only those outmigrants with certain information were analyzed, the standardized incidence ratios did not increase. This has important implications about our conclusions regarding the entire Index Area 1970 cohort; in particular, it is apparent from these latter data that any inaccuracies in a small number of outmigrants could not have caused us to fail to detect a significant increase in cancers.

15.2.2 Stratification by Length of Residence

One of the potential deficiencies of utilizing the Index Area 1970 cohort in the primary test of hypothesis is that this cohort contains individuals who may have entered the area just prior to 1970 and, therefore, may not have had reasonable durations of exposure. One might argue, for example, that any putative risk associated with environmental exposures beginning in 1957 might be diluted if individuals with short exposures were included in the analysis.

To test this, we conducted a secondary analysis in which only individuals with maximal durations of exposure were considered. The first sour gas plant in the Index Area began operation in 1957 so that a member of the Index Area 1970 cohort could have had no more than 13 years of exposure prior to 1970. The results in this section pertain to a secondary analysis in which only individuals with the full 13 years of prior exposure were included. For convenience, we will refer to such individuals as "fully exposed".

There were a total of 105.3 cancers expected in the fully exposed Index Area 1970 cohort and a total of 113 observed incident cancers in the latter group. These data give rise to a standardized incidence ratio of 1.07 (0.81, 1.42). Thus, even when individuals with maximal duration of exposure are considered, no excess in cancer incidence is detected.

15.2.3 On the Self-Reporting of Cancer

Every member of the RG participated in the comparative health survey during the summer of 1985. At that time, the RG member completed an extensive interview which included a detailed history of cancer if applicable. In particular, the individual (or his or her parent in the case of a child) was asked to report any history of cancer including type of cancer, date of diagnosis, name and address of any physicians who attended the individual for this cancer, and names of any hospitals in which the individual was treated for this cancer.

Every member of the RG was also linked to the Alberta Cancer Registry as described in section 6.1.4; any member of the RG who reported a history of cancer was separately linked to the Registry by hand and every attempt was made by Registry officials to confirm the reported cancer. For self-reported cancers that could not be confirmed by the Alberta Cancer Registry, we contacted the physicians who were identified as having cared for the individual for the reported cancer; the attending physicians were asked to confirm the history of cancer, the type of cancer, and the date of diagnosis. If necessary, hospitals where the individual may have been admitted for the cancer were also contacted to confirm the reported information.

When the self-reported histories of cancer in the RG are compared against the information obtained from the Cancer Registry and from attending physicians (where applicable), some insight into the reliability of the self-reported histories of cancer can be obtained. A total of 47 individuals in the RG reported a history of cancer. A total of 29 incident cancers (diagnosed during the period 1970-84) were confirmed in 28 of these individuals; there was one individual with 2 confirmed incident cancers. These 29 confirmed incident cancers included 15 basal cell carcinomas of the skin, 3 cancers of the breast, 2 cancers of the lip, 2 cancers of the rectum, 1 primary liver cell cancer, 3 cancers of the prostate, 1 cancer of the uterus, 1 cancer of the kidney, and 1 melanoma. Six individuals who did not report a history of cancer during the questionnaire were found via the linkage to have had an incident cancer. Five of these were basal cell carcinomas of the skin and one was a cancer of the bladder. This accounts for the total of 35 incident cancers in the RG as seen in Table 15.1.3/1.

Thus, of 47 individuals who reported a history of cancer, 28 were subsequently confirmed to have had incident cancers. The remaining 19 cases included 9 cancers which fell outside the Incidence Period (6 confirmed, 3 unconfirmed) and 4 self-reported cancers which were identified by the Registry as being either benign or in-situ lesions including 1 benign cyst of the parotid gland, 1 benign breast cyst, and 2 in-situ lesions of the cervix. The remaining 6 self-reported cancers could not be linked at all by the Alberta Cancer Registry and so attending physicians were contacted to obtain the following information: one woman who reported a cancer of the skin was found to have had an actinic keratosis; one man had a basal cell cancer of the skin but an exact date of diagnosis could not be obtained; one woman who reported a cancer of the uterus was found to have had a non-confirmatory cone biopsy of the cervix followed by a hysterectomy; one man who reported having lung cancer was found to have had a granuloma of the lung; one woman who reported a cancer of the uterus was found to have had an in-situ lesion of the cervix with a subsequent hysterectomy; and one individual reported a cancer of the skin which was not confirmed by either the Alberta Cancer Registry or by the attending physician named in the questionnaire.

Thus, in summary, there were a total of 12 out of 47 (26%) members of the RG who reported themselves to have cancer but whose diagnosis on follow-up with the Alberta Cancer Registry or with attending physicians, turned out to be a benign lesion (4), an in-situ lesion (3), or could not be confirmed (5).

15.2.4 Analysis by Site

We undertook several analyses with respect to various cancer sites. However, before presenting these data, several cautions must be raised. First, only the overall cancer experience of the Index Area 1970 cohort was specified to be involved in the primary hypothesis test in this study. No one in the community at any time prior to this study singled out a particular cancer site as being of special interest. Thus, any analysis of sites must be viewed in the light of multiple comparisons. Second, *a priori* sample size and power considerations for this study were made in the light of overall cancer incidence rates. It was never purported or intended that this study would have adequate power to investigate specific sites. Third, with the exception of non-melanotic skin cancer which has already been observed to be increased in parts of Southern Alberta and lung cancer which was anticipated to be low in this area due to the low rate of smoking, there were no other sites for which we had any pre-existing evidence to suspect any increases or decreases in the Index Area 1970 cohort. Fourth, it was recognized at the outset that site-specific incidence rates for the reference populations would not be reliable as these would be based on small numbers of observed cases. Thus for site-specific analyses (with the exception of non-melanotic skin cancers), we were compelled to use the entire population of Alberta as the reference population with a resultant loss of comparability.

With regard to non-melanotic skin cancers, there were 45 such cancers observed in the Index Area 1970 cohort whereas there were 31.4, 29.3, and 31.7 such cancers expected based on rates from the 3 reference populations. These data give rise to standardized incidence ratios for non-melanotic skin cancers in the Index Area 1970 cohort of 1.43 (0.90, 2.35), 1.54 (0.95, 2.54), and 1.42 (0.91, 2.35) respectively. These elevations do not reach statistical significance.

Because a relatively large proportion of the Index Area population consists of non smokers, we anticipated there might be a deficit of respiratory cancers (larynx, trachea, bronchus, lung). There were 6 such incident cancers observed in the Index Area 1970 cohort while based on general Alberta incidence rates, 12.1 cases were expected. Thus the standardized incidence ratio for respiratory cancers is 0.50 (0.20, 1.24).

There were no statistically significant deviations between observed and expected numbers of cancers for any other sites. The only non-trivial excess noted was for prostate cancer where 10.8 cases were expected and 19 were observed. These data yield an SIR of 1.76 (0.84, 4.38). Given that this excess is not statistically significant, given the number of comparisons made in the site-specific analysis, and given the lack of any prior evidence about an association between sour gas and prostate cancer, there is no reason to believe that this non-significant excess is anything other than a chance observation.

15.2.5 Age at Diagnosis

We also undertook an investigation which considered the age of individuals at the time of diagnosis of their first malignancy. It could be argued, for example, that if some environmental agent were at work in the Index Area 1970 cohort then their distribution of age at diagnosis of first malignancy might be different than that of a reference population.

Non-melanotic skin cancers were excluded in this analysis. The mean age of individuals at the time of diagnosis of their first malignancy in the Index Area 1970 cohort during the period 1970-84 was 64.2 years. The mean age at diagnosis for all first malignancies diagnosed in reference population 1 (non-metropolitan Southern Alberta) during the period 1970-84 was 63.91 years. No differences in the age distributions were detected.

15.2.6 Analysis by Sub-Area Within the IA

To study any possible relationship with intensity of exposure, we undertook several secondary analyses stratified by area of residence within the Index Area. It should be noted that at the time of the visit to the comparative health survey, all participants were asked to mark their place of residence on a map. This information was used to give each participant a geographical ID code. Thus accurate information on place of residence within the Index Area is available for each RG member. However, data concerning exact location of residence within the Index Area are not reliable or complete for the OG. Therefore, in all analyses regarding area of residence we have only utilized the RG. Prior to analysis of the data, the Community Advisory Board was asked to delineate those areas within the Index Area considered to receive the greatest exposure to sour gas emissions. By comparing the area they delineated with the geographic ID codes, it was possible to determine whether an RG member was living in an area of high exposure. For convenience, we will refer to such individuals as "highly exposed". There was 19 individuals for whom geographic ID codes were not available. The highly exposed area as delineated by the Community Advisory Board contained 124 individuals comprising 12.4% of the RG. The total number of expected incident cancers among the highly exposed RG members was 5, based on rates from reference population 1. Among highly exposed RG members only 1 incident cancer was observed, a basal cell carcinoma of the skin. Although these numbers are too small for any formal statistical analysis, it does not appear that there is any undue incidence of cancer among highly exposed individuals.

We conducted a second analysis by area in which we divided the Index Area into 5 zones which were meant to encompass the areas around the 5 towns within the Index Area (Twin Butte, Glenwood, Hill Spring, Mountain View, and Willow Creek). For this analysis, we excluded non-melanotic skin cancers. Zone 1 (consisting of geographic ID areas 1 through 34) had a total of 5 incident cancers (12.9 expected). Zone 2 (geographic ID areas 35 - 38) had 4 incident cancers (8.6 expected). Zone 3 (comprising geographic ID areas 39 - 42) had 3 observed incident cancers (9.1 expected). Zone 4 (comprising geographic ID areas 43 - 52) had 2 observed incident cancers (8.2 expected). Finally, Zone 5 (comprising geographic ID areas 53 - 63) had 0 observed incident cancers (2.4 expected). It should be noted that all expected numbers of cancers were computed using rates from reference population 1 (non-metropolitan Southern Alberta). Again, these numbers are too few for formal statistical analysis but it is apparent that there is little disparity in cancer incidence among the 5 zones defined within the Index Area.

15.2.7 Supplemental Incidence Period

As noted earlier, the calendar year 1985 was analyzed separately for several reasons. First, because of a delay between the time of diagnosis of a cancer and the time that such a cancer is registered in the Alberta Cancer Registry, records for the year 1985 are even at this time incomplete. Second, because every RG member underwent a full multiphasic health examination with subsequent secondary and tertiary referral, this process might be anticipated to have uncovered some occult cancers at an early stage which might cause an artificial rise in the 1985 cancer incidence for the Index Area. As noted earlier, we conducted a separate linkage to the Alberta Cancer Registry dated April 4, 1986 for the purpose of investigating cancers which were diagnosed during the year 1985.

It should be noted that for this analysis, we included not only the entire Index Area 1970 cohort but also all current residents of the Index Area as well. Thus, current residents of the Index Area who were not present in the area in 1970 were also studied.

Three cancers were detected in the OG during the year 1985. These included 2 basal cell carcinomas and 1 colorectal cancer.

In addition, 2 in-situ carcinomas of the cervix were reported in the OG as well for 1985. There were 5 cancers detected in the RG during the year 1985; these included 1 basal cell carcinoma, 2 cancers of the prostate, 1 cholangiocarcinoma, and 1 melanoma. As well, there were 2 cancers identified among current residents of the Index Area who were not members of the RG by virtue of the fact that they were not present during the year 1970. These included 1 basal cell carcinoma and 1 cancer of the breast. Thus there were a total of 10 cancers diagnosed in 1985 in these latter 3 groups. Based on the age distribution of these 3 groups and based on the assignment of 1 person-year of risk to each individual, there were a total of 18.1 cancers expected during 1985 utilizing rates for reference population 1 for the period 1980-84. We have received additional reports from the Community Advisory Board about 3 "possible" cancers currently being investigated. Even when these are included, the total of observed cancers is only 13. Thus there would appear to be a deficit of cancers during 1985 in the observed population. This would most likely be due to a delay in the reporting of diagnosed cancers from 1985. At the very least, there is no evidence to suggest that there has been any undue excess in cancer incidence among residents of the Index Area during the year 1985.

15.3 Observations on the Cancer Incidence Study

There are several observations to be made about the Cancer Incidence Study component of the Southwest Alberta Medical Diagnostic Review Project. The purpose of this section is to discuss some of the observations and some of the limitations of this component of the study.

15.3.1 Accuracy of the Outmigrant Group

A fundamental issue concerns the accuracy of the enumeration of the Outmigrant Group and hence the accuracy of our estimate of person-years of risk. The difficulties associated with enumerating this group are discussed in detail in section 4.3.4.1 as are the steps that were taken in the enumeration process. A review of these steps should indicate that we used every conceivable means at our disposal to enumerate the Outmigrant Group. It must be pointed out, however, that there is no "gold standard" against which we can assess the accuracy of our enumeration. However, there are several observations which can be made which can help to assure its overall accuracy:

1) Only outmigrants who were identified by two independent sources were utilized in the analysis. The vast majority of the outmigrants were replicated by several sources; such

replication serves to assure the accuracy of the information regarding the outmigrant. As well, each outmigrant was reviewed by the Outmigrant Review Panel (see section 4.3.4.1) which was identified by the community as being local experts on past residents of the area.

2) We obtained complete outmigrant information for a total of 1,163 individuals in the Outmigrant Group. As noted above, there is no "gold standard" against which to assess the accuracy of this total. However, it should be pointed out that this total gives rise to an overall estimate of 2,164 for the size of the Index Area 1970 cohort. Given the current population estimate for the Index Area of about 2,327 and given an elapsed interval of fifteen years, we believe the total of 2,164 represents a realistic estimate of the population of the Index Area in 1970. This provides some additional assurance about the accuracy of the Outmigrant Group. With regard to our enumeration process which relied heavily on the recall of current residents of the Index Area, one might argue that those outmigrants who subsequently suffered an unfortunate event such as developing cancer are more likely to be recalled by their friends and relatives by virtue of this event. Thus, our enumeration process may slightly bias the Outmigrant Group towards those more likely rather than less likely to develop cancer.

3) The reader will recall from section 6.1.3.2 that a certainty code was assigned to each outmigrant. The definition of the certainty code is given in section 6.1.3.2 and is meant to reflect the overall accuracy of the information regarding that outmigrant. Two important points should be raised in this regard. First, we adopted the a priori policy that when there were incongruous sets of data of equal quality regarding an outmigrant, the one which gave rise to a lower total person-years of risk was chosen. Thus, if any error was introduced, it was such that person-years of risk and hence numbers of expected cancers would be lowered, and hence standardized incidence ratios would be elevated. This strategy would favour the likelihood of finding an elevated incidence in the Index Area. Second, we performed separate analyses stratified by certainty code. In particular, when only those individuals with certainty codes of 1 were included in the analysis, there was no significant change in the results. This indicates that inaccuracy of information in a small number of outmigrants could not have biased the outcome of the study.

4) It is also important to note that every decision regarding the editing of the outmigrant file including the assignment of certainty codes was performed without any knowledge of

subsequent cancer experience. Thus no systematic bias could be introduced by the editing with the exception of the liberal biases described above which were adopted to lower total person-years of risk whenever discretionary choices were made.

15.3.2 Restriction within Alberta

It must be acknowledged that the Cancer Incidence Study is restricted to cancers diagnosed within Alberta. Thus it is the cancer experience of the Index Area 1970 cohort while they remain within Alberta that is being investigated. This was done because the Alberta Cancer Registry which was our main source of incident cancer information, registers cancers diagnosed within the province of Alberta. Person-years of risk were adjusted accordingly; only person-years of life within Alberta were used in the calculations. For the restriction to Alberta to bias our results, one would have to postulate that those outmigrants from the Index Area 1970 cohort who leave the province of Alberta are more or less likely to develop cancer than those outmigrants who leave the Index Area but remain within the Province of Alberta. There are no data to support such an unlikely and complicated hypothesis; therefore, we see no reason why the restriction to within Alberta should affect the results of this study.

15.3.3 Use of the Alberta Cancer Registry

The Alberta Cancer Registry is one of the most comprehensive, accurate, and up to date of such existing registries in operation. Their records are updated on a continuing basis. In addition, they have had extensive experience with computerized record linkage. However, it must be recognized that any cancer registry will inevitably miss some cancers in its catchment. This is especially so for lesions such as carcinoma-in-situ and for relatively innocuous cancers such as basal cell carcinoma of the skin. In addition, it is virtually inevitable that there will be some occasional inaccuracies with regard to ICD-9, date of diagnosis, date of death, etc., due to reporting error, coding error, and/or data entry error. It is important to point out, however, that if there are any systematic inaccuracies in the Alberta Cancer Registry, these will be reflected both in the observed cancers and the expected cancers that we utilized. This is so because the Alberta Cancer Registry supplied both the incident cancers from the Index Area 1970 cohort and the cancer incidence rates from the reference populations. Thus, there is no reason to believe that use of the Alberta Cancer Registry as our source of both observed and expected cancers could give rise to any distorted effects on the results of this study.

16. REPRODUCTIVE RISKS AND OUTCOMES

16.1 Sociodemographic Information

In this chapter we present the data on reproductive risks and outcomes. The various outcome measures to be used in this study component employ different definitions of "population at risk". Also, different potential confounders were identified for each outcome. Consequently, to assess the comparability of the groups for the analysis of these reproductive outcomes, we present sociodemographic comparisons between women of child bearing age in the comparison areas, and women with at least one pregnancy. We will also show the distribution of sociodemographic characteristics for all children under 15 examined during the summer 1985 survey, that is, the population at risk defined for the assessment of inadequate childhood development. Corresponding information from the outmigrants will also be assessed.

In Table 16.1/1 we present selected sociodemographic variables for women who spent at least one year of childbearing age in the areas under study sometime between 1957 and 1985. These data pertain only to the participants in the summer health survey. The populations for the Index Area and for SR are similar with regard to religion. It is noted that there is a

TABLE 16.1/1

SUMMER 1985 SAMPLES
SELECTED SOCIODEMOGRAPHIC VARIABLES FOR WOMEN OF CHILD BEARING AGE BETWEEN 1957 AND 1985 BY AREA

	AREA			
	IA	SR*	DCCI*	SR-M*
N	617	262	293	146
Distribution by Age in 1985				
15-29	29.0	27.5	25.3	25.3
30-44	31.8	47.0	49.2	48.0
45-64	29.3	21.8	16.4	24.7
Mean Age	41.2	37.3	38.8	37.0
Distribution by Religion				
United	15.6	4.6	28.3	8.2
Catholic	15.4	16.0	15.7	28.8
Mormons	46.0	44.3	0.7	0.0
Other	22.7	24.4	46.8	43.8
No response	0.3	10.7	8.5	19.2
Length of Residence (Years)				
Mean	23.8	18.2	18.3	16.7
Median	19.0	14.5	11.0	15.5

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* Includes proxies in the Control Areas: mothers who were not in sample, but whose child was.

small shift in the age distribution of the Index Area women towards the older age group.

Table 16.1/2 presents data on selected sociodemographic variables for women who had at least one pregnancy. This again pertains only to women who participated in the summer health survey. Again, in the primary contrast between IA and SR, a small shift in the age distribution towards the older age groups in the IA women is noted.

As noted early in the Methods Section, several questions related to reproductive outcomes were included in the outmigrant questionnaire. The purpose of this was to take into account the experience of the outmigrants in terms of reproductive risks and outcomes and combine it with the residents' experience. Before presenting those outcomes, we show the sociodemographic characteristics of these outmigrants compared to the summer participants.

Table 16.1/3 presents certain sociodemographic variables comparing outmigrant women of child bearing age in the four areas. Because these are data from outmigrants, for the Index Area we use the IA(MC) group, namely the most comparable Index Area outmigrant study group. The comparison between the latter group and the SR group forms the main contrast in these analyses.

TABLE 16.1/2

SUMMER 1985 SAMPLES
SELECTED SOCIODEMOGRAPHIC VARIABLES FOR WOMEN WITH AT LEAST ONE PREGNANCY BETWEEN 1957 AND 1985 BY AREA

	AREA			
	IA	SR*	DCCI*	SR-M*
N	347	165	150	81
Distribution by Age in 1985				
15-29	22.5	21.2	28.0	16.1
30-44	42.1	52.7	52.7	54.3
45-64	29.4	22.4	15.3	25.9
Mean Age	41.2	38.5	36.4	39.3
Distribution by Religion				
United	15.0	4.2	25.3	8.6
Catholic	18.4	13.9	14.7	28.4
Mormons	47.0	50.9	1.3	0.0
Other	19.3	23.0	49.3	46.9
No response	0.3	7.9	9.3	16.1
Length of Residence (Years)				
Mean	24.1	20.1	18.6	20.9
Median	22.0	16.0	12.0	20.0

* Includes proxies in the control areas.

TABLE 16.1/3

OUTMIGRANT RESPONDENTS
SELECTED SOCIODEMOGRAPHIC VARIABLES FOR WOMEN OF CHILD BEARING AGE BETWEEN 1957 AND 1985 BY AREA

	AREA			
	IA(MC)*	SR	DCCI	SR-M
N	335	132	139	72
Distribution by Age in 1985				
15-29	35.8	34.9	36.0	36.1
30-44	52.2	53.0	56.1	48.6
45-64	10.2	11.4	7.9	13.9
Mean Age	34.3	34.6	33.7	34.9
Distribution by Religion				
United	11.3	7.6	37.4	13.9
Catholic	13.1	18.9	16.6	34.7
Mormons	50.8	45.5	0.7	0.0
Other	20.3	24.2	38.9	44.4
No response	4.5	3.8	6.5	6.9
N	229	82	91	42
Length of Residence (Years)				
Mean	17.9	18.7	17.5	19.7
Median	18.5	19.2	18.3	19.5

* Includes outmigrants who are first degree relatives only.

There is a striking similarity in the age distributions of the IA(MC) and SR groups. These groups are also quite comparable with respect to both religion and to length of residence in their respective areas.

Table 16.1/4 presents a similar comparison between outmigrant women with at least one pregnancy in the four areas. The differences between the groups are certainly related to the very small number of respondents in each cell, and will have only minimal impact once these outmigrants are grouped with the summer participants.

Although the comparison between participants and outmigrants could not be extended to other sociodemographic variables, we can look further at the participants. Indeed we have more information on the summer participants and their similarity across areas with regard to these additional variables is meaningful even after the grouping with outmigrants, since the former group is seven to eight times larger than the latter. Such comparisons between women of childbearing age in the areas are presented in Table 16.1/5. Women in the Index Area as compared to the SR area are remarkably similar. The prevalence of non-smokers is only slightly higher and the number of women with post secondary or higher education is somewhat lower in the IA. In addition, when contrasting the IA and SR populations to the DCCI population, one notes the higher prevalences of women

TABLE 16.1/4

OUTMIGRANT RESPONDENTS
SELECTED SOCIODEMOGRAPHIC VARIABLES
FOR WOMEN WITH AT LEAST ONE PREGNANCY
(Percentage of Women by Area)

	AREA			
	IA(MC)*	SR	DCCI	SR-M
N	56	26	24	9
Distribution by Age in 1985				
15-29	28.6	11.5	20.8	22.2
30-44	48.2	61.5	66.7	33.3
45-64	23.2	26.9	12.5	44.4
Mean Age	37.8	40.7	36.3	43.2
Distribution by Religion				
United	16.1	0.0	45.8	0.0
Catholic	17.9	15.4	12.5	44.4
Mormons	44.6	65.4	0.0	0.0
Other	19.6	15.4	37.5	44.4
No response	1.8	3.9	4.2	11.1
N				
Length of Residence (Years)				
Mean	19.1	15.6	19.3	10.8
Median	19.8	18.0	20.0	6.8

* Includes outmigrants who are first degree relatives only.

TABLE 16.1/5

SUMMER 1985 SAMPLES
SELECTED SOCIODEMOGRAPHIC VARIABLES FOR WOMEN OF CHILD BEARING AGE BETWEEN 1957 AND 1985 BY AREA

	AREA			
	IA	SR*	DCCI*	SR-M*
N	617	262	293	146
Married	79.3	78.6	83.3	76.0
Mormons	46.0	44.3	0.7	0.0
Never Used Alcohol	43.8	42.4	11.26	16.44
Never Smoked	74.6	69.3**	48.5**	59.7**
Never Used Oral Contraceptives	45.1	41.0	29.8	35.9
Never Used Other Contraceptives	51.9	55.6	52.9	60.7
Family Income $20,000 and more	53.7	58.0	68.3	56.9
Education post secondary or higher	24.5	31.3	29.3	28.1

* Includes proxies in the control areas.
** Denominators slightly smaller, information not available for proxies.

who have never used alcohol, who have never smoked and who have never used oral contraceptives in the former two groups.

In Table 16.1/6 we present similar comparisons among women who have had at least one pregnancy. In the main contrast between IA and SR, the only noticeable difference is in the smoking history where IA women have a higher prevalence of never-smokers.

Table 16.1/7 presents comparisons between the children and their parents amongst the four study areas. With regard to the main contrast between IA and SR, the largest difference noted (13.5%) is the difference in the number of mothers who never smoked. There is a mild shift in the age of the mother at the birth of the child toward the younger age group in the IA as well. The differences in the mothers education is difficult to interpret in view of the differential rate of reporting.

Table 16.1/8 presents the pattern of contraceptive use among women in the four areas by decade of birth. One notes in this Table an increasing prevalence of use with later date of birth. There is a uniform decrease in the prevalence of contraceptive use of women born in the 60's across all four areas therefore delayed first pregnancy is not commonplace. However, the most important feature of this Table is the similarity in the pattern of contraceptive use across the four study areas.

TABLE 16.1/6

SUMMER 1985 SAMPLES
SELECTED SOCIODEMOGRAPHIC VARIABLES FOR WOMEN WITH AT LEAST ONE PREGNANCY BETWEEN 1957 AND 1985 BY AREA

	AREA			
	IA	SR*	DCCI*	SR-M*
N	347	163	150	81
Married	91.9	92.6	93.3	91.3
Mormons	47.0	50.9	1.3	0.0
Never Used Alcohol	41.8	41.2	10.7	11.1
Never Smoked	73.2	65.0**	54.6**	49.2**
Never Used Oral Contraceptives	36.3	32.5	20.3	28.8
Never Used Other Contraceptives	41.8	48.5	43.0	58.8
Family Income $20,000 and more	59.1*	61.2	69.3	56.8
Education post secondary or higher	27.7	33.3	28.7	28.4

* Includes proxies in the control areas.
** Denominators slightly smaller, information not available for proxies.

Table 16.1/7

SUMMER 1985 SAMPLES SOCIODEMOGRAPHIC CHARACTERISTICS RELATED TO CHILDREN (UNDER 18) EXAMINED IN THIS STUDY BY AREA*
(Distribution in %)

	AREA			
Age of mother at birth of child	IA	SR	DCCI	SR-M
<25	37.0	32.5	31.3	36.9
25-35	52.9	60.3	65.4	58.2
>35	10.1	7.2	3.3	4.9
Mothers use of alcohol				
Never	47.9	40.2	9.4	14.1
Ever	52.1	59.8	90.6	85.9
Smoking in mothers				
Never	74.8	61.3	37.7	42.4
Ever	25.2	38.7	62.3	57.6
Mothers education				
≤ 6 years	1.2	1.5	0.4	2.9
7 to some sec.	61.9	48.4	56.9	54.1
Post sec. or higher	30.2	30.9	33.7	25.9
Not reporting	6.7	19.2	9.0	17.1
Family income				
<9,000	2.8*	2.9	1.5	3.5
9,000-20,000	19.2	11.4	11.2	10.0
>20,000	62.5	53.9	71.9	54.1
not reporting	15.6	31.8	15.36	32.4
Child sex				
Male	51.7	46.9	48.7	51.2
Father's occupation				
Farmer	48.7	39.7	28.8	48.2
Other	51.3	60.3	71.2	51.8
Age groups of children at examinations				
0-5	38.5	40.5	46.2	27.1
6-9	29.9	34.4	28.6	41.8
10-14	31.6	25.1	25.2	31.1

* In ritualistic medical examinations the age cut-off for children was 18.

TABLE 16.1/8

PERCENTAGE OF WOMEN EVER USING CONTRACEPTIVES BY DECADE OF BIRTH

	AREA							
	IA		SR		DCCI		SR-M	
N	662		221		182		130	
Decades of Women's birth	%	N	%	N	%	N	%	N
≤ 1910's	45	60	9	11	46	26	0	4
1920's	61	94	59	22	61	28	45	11
1930's	70	98	68	34	61	18	61	23
1940's	90	123	94	52	87	38	93	30
1950's	92	152	84	58	94	31	91	35
1960's	44	135	31	48	56	41	37	27
Combined	**70**	**662**	**68**	**221**	**69**	**182**	**68**	**130**

All this sociodemographic information suggests that the residents of the three areas studied in 1985 are reasonably similar with regard to a large number of key variables. In addition, these residents are very similar to their first degree relatives who left the respective areas with regard to a smaller number of key items (age, religion, length of residence).

As seen earlier, these outmigrants left the area mostly for education, work or to create a family elsewhere. They left their respective areas at a comparable average age varying between 21.4 and 22.9. This will limit necessarily their reproductive experience in the areas under study.

This information helps in the understanding of the contribution that these outmigrants have in the analysis of the reproductive outcomes. Indeed, wherever possible, the following analysis looks only at the resident and outmigrant data combined within each area. This represents the best estimate of the true reproductive experience in these areas.

Since the data are based essentially on self reports that have not been verified or objectively confirmed, the analysis will focus on indicators less susceptible to response bias and to small sample sizes. These indicators will appear under the following headings: fertility and fetal losses, low birth weight, congenital anomalies, and childhood development.

16.2 Fertility and Fetal Losses

Table 16.2/1 presents the proportion of females reporting any fertility problems in the family by age at the time of the problem. There is an approximately 3.2% higher prevalence of such problems in the IA as compared to the SR. However, there is no difference between the prevalence of such reports in DCCI as compared to SR-M.

The same question was asked to males; a lower percentage of them report fertility problems and the difference between the areas is smaller.

Fertility, which we have defined to be the number of live births per 1000 women-year of child bearing age spent in a particular area, is analyzed in Table 16.2/2. There were no clinically significant differences in fertility between the IA and SR with respective rates of 102.8‰ and 126.3‰. It is interesting to note that the fertility of the SR drops from 126.3‰ to 89.9‰ when Mormon women are excluded. This suggests that the fertility rate for Mormon women is much higher than 126.3‰ and serves as an indicator that the influence of the Mormon population in this particular analysis is considerable. Also, the lower fertility rates in mothers less than 20 years of age in IA and DCCI, should be interpreted in the light of the

TABLE 16.2/1

PERCENTAGE OF FEMALES REPORTING ANY FERTILITY PROBLEMS BY AGE OF FEMALE AT TIME OF PROBLEM

(Participants Only)

	AREA			
	IA	SR	DCCI	SR-M
N	649	221	190	131
Age of female at time of problem				
< 20	1.69	1.36	0	2.31
20-24	5.08	4.98	5.03	3.08
25-29	3.24	1.81	2.23	2.31
30-34	0.46	0	0.56	0
35-39	0.31	0.45	0.56	0.77
≥ 40	0.46	0	0	0
Combined	**11.86**	**8.60**	**8.38**	**8.47**

TABLE 16.2/2

AGE SPECIFIC FERTILITY RATES PER 1000 WOMEN-YEARS IN PARTICIPANTS AND OUTMIGRANTS BETWEEN 1958 AND 1985

Age of Mother at Time of Pregnancy	AREA							
	IA		SR		DCCI		SR-M	
	‰	N	‰	N	‰	N	‰	N
< 20	19.5	1744	38.7	697	20.1	697	29.5	375
20-24	245.5	1136	225.6	532	182.5	526	163.5	263
25-29	241.3	1239	245.2	620	198.2	560	198.2	328
30-34	128.6	1252	171.0	649	85.4	515	125.7	350
35-39	74.0	1217	78.6	496	30.7	391	30.8	292
> 40	17.1	2169	11.2	624	9.8	712	18.2	384
Combined	**102.8**	**8757**	**126.3**	**3618**	**83.5**	**3401**	**89.9**	**1990**

more frequent use of contraceptives in females of that age group in these areas (see Table 16.1/8). Table 16.2/3 contrasts the observed number of live births in the respective areas with the number expected when using the age and period specific fertility rates of Albertan women of childbearing age. The observed numbers are invariably larger than the expected.

Table 16.2/4 presents the proportion of pregnancies reported to have led to fetal losses by the age of the mother at the time of the loss. There is a 3% higher prevalence of reported fetal losses in the IA as compared to the SR. The largest difference found was between SR and IA for the youngest age groups. It is noteworthy that there were no reported fetal losses in the youngest age group in either DCCI or SR-M. Because we are dealing with small numbers in this age group, the differences did not reach statistical significance. The statement and reason also apply to the differences between DCCI and SR-M in age groups 40-44 and 45-49.

Furthermore, in the two areas where more fetal losses were observed, IA and DCCI, more of these fetal losses occurred after a first miscarriage or in women with habitual spontaneous abortions. Table 16.2/5 shows this finding and also the impact of excluding from IA and DCCI data, respectively two and one mothers with very large numbers of fetal losses. There were no mothers with large numbers of fetal losses in the other areas.

TABLE 16.2/3

STANDARDIZED FERTILITY RATIOS IN PARTICIPANTS AND OUTMIGRANTS

	AREA							
	IA		SR		DCCI		SR-M	
	Obs.	Exp.	Obs.	Exp.	Obs.	Exp.	Obs.	Exp.
Number of Live Births	900	664	457	302	284	249	179	163
Age and Period Standardized Fertility Ratio*	1.35		1.51		1.14		1.10	

* Reference population: population of Alberta in 1960, 1969, 1976 and 1983.

TABLE 16.2/4

PROPORTION (%) OF PREGNANCIES LEADING TO REPORTED FETAL LOSSES IN PARTICIPANTS AND OUTMIGRANTS

Age of Mother at Time of Loss	AREA							
	IA		SR		DCCI		SR-M	
	%	N	%	N	%	N	%	N
< 20	21.7	46	3.4	29	0	20	0	11
20-24	11.8	323	12.1	140	17.8	118	18.5	54
25-29	15.4	357	9.5	169	14.0	129	14.3	77
30-34	14.6	192	11.7	128	15.4	52	13.2	53
35-39	13.2	106	18.8	48	14.3	14	10.0	10
40-44	25.5	47	33.3	9	22.2	9	0	6
45-49	33.3	3	33.3	3	0	0	50	2
Combined	**14.7**	**1074**	**11.8**	**526**	**15.1**	**338**	**13.9**	**216**

TABLE 16.2/5

CONTRIBUTION OF HABITUAL SPONTANEOUS ABORTION (%) IN FETAL LOSSES

	AREA			
	IA	SR	DCCI	SR-M
Women with at least one pregnancy, N	347	163	150	81
Percentage of N with one miscarriage	24.2	20.6	20.7	23.5
Percentage of N with at least two miscarriages	9.5	6.6	8.0	6.1
Percentage of miscarriages occurring after a first miscarriage	40*	26	35**	23

* 31% if we exclude two mothers with multiple abortions.

** 21% if we exclude one mother with multiple abortions.

16.3 Low Birth Weight

Table 16.3/1 gives the percentage of all live births with a weight less than 5.5 pounds. According to this definition, the occurrence of low birth weight is similar in IA and SR and the lowest in DCCI. Although based on reports by the mothers, this information, with the report of births themselves, is probably the least susceptible to response bias.

TABLE 16.3/1

PROPORTION OF LOW BIRTH WEIGHTS AMONG ALL LIVE BIRTHS BY MARITAL STATUS IN PARTICIPANTS (< 5.5 LBS)

	AREA							
MARITAL STATUS	IA		SR		DCCI		SR-M	
	%	N	%	N	%	N	%	N
Never Married	0	2	0	4	0	0	0	2
Ever Married	5.0	859	5.0	419	3.8	261	8.4	167
Combined	**5.0**	**861**	**5.0**	**423**	**3.8**	**261**	**8.3**	**169**

16.4 Congenital Anomalies

Data pertaining to the percentage of participants noted to have at least one congenital anomaly either on judgemental clinical examination or on consultation with the appropriate medical specialist, are presented in Table 16.4/1. It is noted that the prevalence of such anomalies are both low and comparable across all four areas.

The percentages of deliveries leading to birth defects as reported by participants in the health survey are presented in Table 16.4/2. The crude proportions of such deliveries were slightly different, the IA groups with a prevalences of 6.3% and the SR group with 4.6%.

To minimize the effect of any response bias we looked at the occurrence of major birth defects in IA and SR and DCCI. We compared the numbers observed to the numbers expected when we apply to our study groups the condition specific rates measured from the experience of the general population in Manitoba, in 1985. The numbers shown in Table 16.4/3 are remarkably similar. The difference between observed and expected in DCCI is still within the confidence limits because the numbers are so small. In this Table, the numbers observed are based on the reports from the mothers, from the judgemental examination and/or from the consultations with the appropriate medical specialists.

TABLE 16.4/1

PERCENTAGE OF PARTICIPANTS WITH AT LEAST ONE EARLY CONGENITAL ANOMALY BY JUDGEMENTAL AND CONSULTATION

	AREA			
	IA	SR	DCCI	SR-M
All Participants				
N	2153	821	611	458
Percentage with Anomaly	1.6	2.1	1.3	2.6
Participants Born in the Areas				
N	797	308	199	159
Percentage with Anomaly	1.9	3.3	1.0	5.0

TABLE 16.4/2

PROPORTION OF DELIVERIES (%) REPORTED IN OUTMIGRANTS AND PARTICIPANTS AS LEADING TO BIRTH DEFECTS

	AREA							
	IA		SR		DCCI		SR-M	
Age of Mother at Time of Delivery	%	N	%	N	%	N	%	N
< 20	8.8	34	7.4	27	0	14	0	11
20-24	7.2	278	3.3	120	5.2	96	0	44
25-29	5.3	303	7.2	152	6.3	110	4.6	65
30-34	6.2	161	1.8	109	2.2	44	4.5	44
35-39	6.5	91	2.5	40	7.6	13	0	9
> 40	5.4	37	14.3	7	0	7	14.3	7
Combined	**6.3**	**904**	**4.6**	**457**	**4.9**	**284**	**3.3**	**180**

TABLE 16.4/3

OBSERVED MAJOR BIRTH DEFECTS IN PARTICIPANTS AND OUTMIGRANTS COMPARED TO EXPECTED NUMBERS, BETWEEN 1957 AND 1985

	AREA					
	IA		SR		DCCI	
N	906		466		285	
	OBS.	EXP.*	OBS.	EXP.*	OBS.	EXP.*
Neural tube defects	0	1.0	0	0.5	0	0.3
Hydrocephalus	0	0.6	0	0.3	0	0.2
Cleft lip	1	0.7	1	0.3	0	0.2
Cleft palate	1	0.5	2	0.2	0	0.1
Pyloric stenosis	5	2.1	1	1.1	2	0.7
Hypospadias	2	1.7	1	0.9	0	0.5
Congenital hip dysplasia	7	7.6	1	3.9	0	2.4
Downs syndrome	1	1.4	1	0.7	0	0.4
Anomalies of septal closure	2	4.1	3	2.1	0	1.2
Total	19	19.7	10	10.0	2	6.0
Observed to expected ratio (OER)	0.96		1.00		0.33	
95% confidence interval for OER	0.58 - 1.51		0.48 - 1.84		0.04 - 1.20	

* Based on rates for each condition in the population of Manitoba in 1985.

16.5 Childhood Development

Table 16.5/1 displays developmental characteristics of children as reported by parents through the questionnaire, and therefore dependent on the parents' memory. There are no differences of practical importance among areas, notably IA compared to SR.

When we consider infant development in the aggregate, we see that fewer boys in IA and DCCI have "no delay" compared to the other areas. On the other hand, fewer girls have "no delay" in SR-M. Parents' satisfaction with their children's development is slightly better for girls than for boys and is comparable across the areas.

Table 16.5/2 displays our findings regarding the developmental characteristics of children which were objectively measured in the field. We would expect 5% of all children to fall below the fifth centile for height and weight. This was slightly exceeded in DCCI for height and weight and for SR for height and has no clinical significance in either instance. Examining the DCCI findings more closely, we see that it is primarily the girls who tend to be below the fifth centile for height and weight, whereas the boys tendency is in the opposite direction.

The Denver Developmental Screening Test scores administered to children at age four were essentially equal across all areas, although they tended to be higher for IA and DCCI.

The development of secondary sexual characteristics in teenagers as measured during the ritualistic medical examination showed no differences across areas although the IA tended to show fewer delays in boys and slightly more delays in girls.

In summary, no clinically significant differences between areas were found in any of the developmental data (Tables 16.5/1 and 16.5/2).

TABLE 16.5/1

PERCENTAGE OF DEVELOPMENTAL CHARACTERISTICS OF CHILDREN (%)

		AREA			
		IA	SR	DCCI	SR-M
Infant Development:					
Roll Over	Boys	100.0	100.0	100.0	100.0
	Girls	100.0	100.0	100.0	100.0
Sitting	Boys	96.7	98.2	98.0	100.0
	Girls	98.0	96.7	100.0	92.9
Walking	Boys	96.7	96.3	100.0	93.3
	Girls	97.4	100.0	96.5	100.0
Infant Development:					
Boys percent	no delay	73.3	83.3	62.0	86.7
	one delay	24.2	14.8	38.0	13.3
	two delays	2.5	0.0	0.0	0.0
	three delays	0.0	1.9	0.0	0.0
Girls percent	no delay	84.4	82.0	86.0	71.4
	one delay	13.9	18.0	12.3	28.6
	two delays	0.9	0.0	1.8	0.0
	three delays	0.9	0.0	0.0	0.0
Parents Satisfaction with Development:					
Boys	very satisfied	80.8	88.9	90.0	93.3
	somewhat satisfied	15.8	9.3	10.0	6.7
	not satisfied, not worried	0.8	0.0	0.0	0.0
	somewhat worried	0.8	1.9	0.0	0.0
	very worried	0.0	0.0	0.0	0.0
Girls	very satisfied	90.4	95.1	91.2	92.9
	somewhat satisfied	6.1	1.6	5.3	0.0
	not satisfied, not worried	2.6	3.3	1.8	7.1
	somewhat worried	0.9	0.0	0.0	0.0
	very worried	0.0	0.0	0.0	0.0

TABLE 16.5/2

PERCENTAGE OF DEVELOPMENTAL CHARACTERISTICS OF CHILDREN

	AREA			
	IA	SR	DCCI	SR-M
Height below 5th centile (%)				
Boys	4.4	4.5	3.7	3.7
Girls	2.8	6.3	8.2	5.0
Total	3.6	5.4	6.1	4.3
Weight below 5th centile (%)				
Boys	4.6	2.0	1.5	2.8
Girls	4.1	3.4	9.6	3.0
Total	4.4	2.7	5.7	2.8
Delayed Sexual Maturity (%)				
Boys	5.2	5.4	6.7	8.3
Girls	0.9	0.0	0.0	0.0
Denver Developmental Screening Test - Age 4 Years Average Score	21.9	20.4	22.1	19.2

17. MORTALITY

The purpose of this chapter is to set out the results of the analyses relating to the mortality experience of residents of the Index Area. As noted earlier, because of the relatively small sizes of the comparison areas used in this study, we were compelled to construct larger reference areas as described in section 10.3. The reader is referred to section 10.3 for the definitions utilized henceforth in this Chapter.

17.1 Person-Years of Risk

As noted earlier, the person-years of risk used in this analysis are identical to those utilized in the study of cancer risks and outcomes (Chapter 15). The reader will find a more complete discussion of the findings regarding person-years of risk in section 15.1.1. In summary, the Index Area 1970 cohort males experienced a total 15,585 person-years of risk during the period 1970-84. The breakdown of this experience by age group and time interval is presented in Table 15.1.1/2. The Index Area 1970 cohort females experienced a total of 14,590 person-years of risk; a breakdown for the female group by age group and time interval is presented in Table 15.1.1/3.

17.2 Expected Deaths

Table 17.2/1 presents the annual mortality rates per 1000 males by age group and time interval for the two reference areas. A similar table of annual mortality rates for females is presented in Table 17.2/2. As one notes in Table 17.2/1 and 17.2/2, the annual mortality rates in the two reference areas behave as one would expect. First, one notes that in general the rates for females in any given category are lower than the corresponding rates for males. Second, there is an increase in mortality with an increase in age group as one would anticipate. Third, the rates for the lowest age group tend to exceed those of the age group 20-34 due to the high mortality in the first year of life.

One can now apply the appropriate annual mortality rates from Tables 17.2/1 and 17.2/2 to the appropriate person-years of risk as seen in Tables 15.1.1/6 and 15.1.1/7. When these calculations are performed, one derives estimates for the expected numbers of deaths in the Index Area 1970 cohort males of 137.9 and 140.2, and for the Index Area 1970 cohort females of 70.0 and 78.6 based on the two reference area rates respectively.

TABLE 17.2/1

ANNUAL MORTALITY RATES (PER 1000) FOR MALES BY AGE GROUP AND TIME-INTERVAL FOR TWO REFERENCE AREAS

Age Group	1970-74	1975-79 (1977)	1980-84 (1982)
<20	1.91* 2.71**	2.24 1.04	1.42 1.13
20-34	1.83 1.18	1.81 0.94	1.00 2.12
35-44	1.59 2.21	1.79 1.13	1.25 2.91
45-54	5.23 7.36	3.16 1.90	2.37 6.64
54-64	12.70 12.72	14.32 9.14	12.41 14.64
65-69	29.63 23.90	26.75 26.36	33.78 28.36
>70	56.77 65.59	62.46 57.06	67.62 75.54

* Reference Area 1 = Census Division 2 excluding Lethbridge, an area which contains the SR control area.

** Reference Area 2 = Census Division 6 excluding Calgary, an area which contains the DCCI control area.

TABLE 17.2/2

ANNUAL MORTALITY RATES (PER 1000) FOR FEMALES BY AGE GROUP AND TIME-INTERVAL FOR TWO REFERENCE AREAS*

Age Group	1970-74	1975-79 (1977)	1980-84 (1982)
<20	0.71	0.48	0.38
	0.34	1.18	1.88
20-34	0.25	0.94	0.14
	0.51	0.09	0.67
35-44	1.28	1.21	0.33
	2.49	0.92	3.14
45-54	3.08	2.62	4.04
	5.38	3.07	3.46
55-64	5.73	4.87	8.14
	9.29	3.46	10.33
65-69	27.20	14.97	6.91
	17.39	4.42	14.29
>70	52.29	45.52	44.08
	47.62	38.87	61.01

* Reference Area 1 = Census Division 2 excluding Lethbridge, an area which contains the SR control area.

** Reference Area 2 = Census Division 6 excluding Calgary, an area which contains the DCCI control area.

17.3 Standardized Mortality Ratio Analysis

Having set out the basic data, we may now calculate the standardized mortality ratios as previously described. The results of this analysis are presented in Table 17.3/1. A total of 163 deaths (112 male, 51 female) were confirmed by linkage with the records of the Alberta Bureau of Statistics and the Alberta Cancer Registry. In addition, there were 21 reported but unconfirmed deaths in the Outmigrant Group during 1970-84. Nevertheless, these have been included as observed mortalities. In the upper panel of Table 17.3/1, we see the observed and expected numbers of death in the Index Area 1970 cohort males and females respectively. The observed numbers of deaths and the expected numbers of deaths (based on either reference area) are markedly similar. The standardized mortality ratio analysis is presented in the bottom panel of Table 17.3/1. Based on Reference Area 1 which contains SR, there were 207.9 expected deaths while based on Reference Area 2 which contains DCCI, there were 218.8 expected deaths. These data yield standardized mortality ratios of 0.88 (0.73, 1.08) and 0.84 (0.69, 1.03) respectively. The 95% confidence intervals around these estimates indicate that these are not significantly different from unity. Thus, even with unconfirmed deaths imputed to the Index Area 1970 cohort, these data indicate no overall excess in the mortality experience of this cohort. If the unconfirmed deaths are omitted from the analysis, the standardized mortality ratios for the Index Area 1970 cohort are 0.78 (0.64, 0.97) and 0.75 (0.61, 0.92) respectively.

TABLE 17.3/1

STANDARDIZED MORTALITY RATIOS FOR INDEX AREA 1970 COHORT STANDARDIZED TO THE TWO REFERENCE AREAS

Group	Observed Deaths in the Index Area 1970 Cohort	Expected Deaths Based on RA1	Expected Deaths Based on RA
Index Area 1970 Cohort Males	123	137.9	140.2
Index Area 1970 Cohort Females	61	70.0	78.6
Index Area 1970 Cohort Combined	184	207.9	218.8
SMR[*] (95% CI)		0.88 (0.73, 1.08)	
SMR[**] (95% CI)			0.84 (0.69, 1.03)

---

[*] Reference Area 1 = Census Division 2 excluding Lethbridge, an area which contains the SR control area.

[**] Reference Area 2 = Census Division 6 excluding Calgary, an area which contains the DCCI control area.

17.4 Post-Hoc Sample Size Considerations

To summarize the results of the primary mortality analysis, we failed to detect any excess in mortality experienced by the Index Area 1970 cohort relative to the 2 reference areas. In such a circumstance, it is important to consider the possibility of a true excess having been missed due to a Type II error.

Given approximately 215 expected deaths and given a hypothetical SMR for the Index Area as low as 1.2 with alpha = 0.05, the power is 0.88 and 0.80 with a one or two-sided test respectively. Under the same test conditions, the power to detect an SMR of 1.25 is 0.97 and 0.93 with a one and two-sided test respectively. Thus, the probability that we have failed to detect a 20% increase in mortality is small, and the possibility that we have missed an excess as large as 25% is remote.

17.5 Secondary Mortality Analysis

As noted earlier in section 10.3.2.4, because of the concern that rates for subpopulations of Census Divisions might be unstable, we elected to perform a secondary analysis utilizing general Alberta population mortality rates which are considerably more reliable and considerably more stable. Table 17.5/1 presents the annual mortality rates per 1000 males from general Alberta population data set out by age group and time interval. Table 17.5/2 presents similar data for the general Alberta female population. The rates for each time interval have been estimated here by using the middle year rates.

When these mortality rates for the Alberta general population are applied to the appropriate person-years of risk as set out in Tables 15.1.1/2 and 15.1.1/3, one generates the expected number of deaths in the Index Area 1970 cohort over the period 1970-84 based on general Alberta mortality rates. These data are presented in Table 17.5/3. There were a total of 123 deaths (112 confirmed) among Index Area 1970 cohort males with an expected number of deaths of 165.6. There were a total of 61 deaths (52 confirmed) deaths among Index Area 1970 cohort females with an expected number of deaths of 81.6. In the aggregate, there were a total of 184 observed deaths (163 confirmed) with an expected number of 247.2. These data give rise to a standardized mortality ratio of 0.74 (0.61, 0.90). It is noteworthy that the sex-specific standardized mortality ratios are 0.74 and 0.75

TABLE 17.5/1

ANNUAL MORTALITY RATES (PER 1000) FOR MALES BASED ON GENERAL ALBERTA POPULATION BY AGE GROUP AND TIME-INTERVAL

Age Groups	1970-74 (1972)	1975-79 (1977)	1980-84 (1982)
< 20	1.8	3.0	1.2
20-34	1.8	1.9	1.5
35-44	3.0	2.7	2.3
45-54	6.8	6.4	6.0
55-64	16.0	14.7	14.0
65-69	30.8	28.9	29.6
≥ 70	83.7	78.3	77.2

TABLE 17.5/2

ANNUAL MORTALITY RATES (PER 1000) FOR FEMALES BASED ON GENERAL ALBERTA POPULATION BY AGE GROUP AND TIME-INTERVAL

Age Groups	1970-74 (1972)	1975-79 (1977)	1980-84 (1982)
< 20	1.1	1.0	0.8
20-34	0.6	0.6	0.6
35-44	1.6	1.6	1.4
45-54	3.4	3.0	3.0
55-64	7.7	7.3	7.2
65-69	14.6	14.1	13.2
≥ 70	57.3	54.6	52.8

TABLE 17.5/3

SECONDARY SMR ANALYSIS OF INDEX AREA 1970 COHORT BASED ON GENERAL ALBERTA RATES

Groups	Observed Deaths in the Index Area 1970 Cohort	Expected Deaths Based on Alberta rates	SMR (95% CI)
Index Area 1970 Cohort Males	123*	165.6	0.74 (0.59, 0.95)
Index Area 1970 Cohort Females	61**	81.6	0.75 (0.53, 1.06)
Index Area 1970 Cohort Combined	**184**	**247.2**	**0.74** **(0.61, 0.90)**

* 112 confirmed
** 51 confirmed

respectively for males and females so that the low mortality in this cohort relative to the general Alberta population appears to be evenly distributed to the two sexes.

In summary, the Index Area 1970 cohort has had a favourable mortality experience relative to the general population of Alberta. Even with 21 unconfirmed deaths imputed to the cohort, the SMR is 0.74. If the 21 unconfirmed deaths are excluded, the SMR is lower still at 0.66 (0.54, 0.81). In either case, the deficit in mortality is both demographically important and statistically significant.

18. DISCUSSION

18.1 Recapitulation of Main Objective

We begin this discussion chapter by recapitulating the main general objective of the study. It was to determine whether the residents of the Index Area (IA) experienced adverse health effects more often than is expected from frequencies derived in the most similar unexposed population to the IA, which proved to be the Stirling/Raymond (SR) area. For certain phenomena such as total mortality cancer incidence; where the numbers in the SR area would have been too small and too unstable as a useful control, we used residents of Southern Alberta excluding the main cities, or census subdivisions constructed from subdivisions to simulate the SR control area as closely as possible. We used all of Alberta for comparisons for some contrasts.

Ancillary comparisons were made with an area with residents who were representative of all of Southern Alberta in the Didsbury, Carstairs, Crossfield, Irricana (DCCI) area and also using subsets of the entire Canadian population where similarities or contrasts could be illuminating.

Many types of comparisons have been made. However, for purposes of reaching conclusions we adhere strictly to the procedure proposed and approved in the protocol before we undertook the project. The main comparisons are of IA with the SR area or its most closely resembling aggregate of census subdivisions. Our conclusions are based exclusively on a relatively small number of single composite target variables which were declared in advance.

Such considerations become particularly relevant in our comparisons of individual single variables that form the group we consider "Health Status Evaluation". Accordingly, further comments on matters such as inappropriate multiple comparisons, pre-set criteria for clinical significance, and disparities between subjective and objective findings are found in the preamble of our discussion of health status variables. (Section 18.3.6).

18.2 Overview of Measures to Minimize Bias and to Enhance Reliability of Data

In addition to publishing a simple design of observational, non-experimental research to address the questions about the health of residents in the Index Area, and beyond declaring in advance all the ground rules that we imposed upon ourselves to enhance objectivity of the Medical Diagnostic Review Project, we took exhaustive measures to minimize bias and to increase the reliability of the data. We summarize the most important tactics employed in this chapter.

The Southwest Alberta Medical Diagnostic Review Project was a non-experimental study. The main component of the study was a crossectional survey, while other components required cohort follow-up strategies. Various chapters throughout this report indicate our data-gathering methods and our efforts to control the quality of the design. Here we review all of the tactics employed in the various components of the project that were used to minimize bias and to enhance reliability of data.
It is our opinion that in a non-experimental design, rather than relaxing the rigour of data-gathering methods, it should be tightened in a conscious effort to minimize systematic error. Minimization of bias incorporates and goes beyond enhancement of reliability of data, as will be seen in the following description.

Without elaborating details, which are given elsewhere throughout our report, this summarizes all the appropriate measures:

1) The control areas were meticulously chosen with the most sophisticated geographic and demographic techniques available to insure maximum comparability to IA in this non-experimental design. The principal comparison group to the Index Area, namely the Stirling/Raymond area, was declared in advance to be the main contrast.

2) All data-gathering instruments, questionnaires, and forms for both ritualized and judgemental medical examinations were carefully developed or adapted, tested, and pre-tested in the field, in Montreal. A final "dress rehearsal" of a survey similar to that conducted in Alberta was done in the Eastern Townships of Quebec near the Town of Waterloo for the purpose of identifying and eliminating most problems related to the structure, sequence, and item content of the data-gathering instruments.

3) Data-gatherers (both interviewers and physicians) and all coders, although aware of the general purpose of the Medical Diagnostic Review (MDR), were neither cognizant of the

specific hypotheses of the study nor of the specific intent of any questionnaire or physical examination items employed in the field. This minimized conscious or unconscious interpretation and distortion of observations in the field.

4) The training of all data-gathering staff, including laboratory technicians, could not be lengthy but was very intensive and rigourous. Many checks on the reliability of data-gatherers at all levels were done during training, such as standardized evaluation of clinical findings with use of simulated or standardized patients for physicians, and checks of inter-observer variation during training of pulmonary function technicians. In addition, periodically throughout the summer, the Quebec and Mayo Clinic laboratories analyzed standardized human hair samples of known trace metal concentrations prepared and certified by the National Institute for Environmental Studies in Japan.

5) A 10% sample of laboratory determinations for trace metals were sent to the Mayo Clinic to check the reliability and accuracy of the findings from the Centre de Toxicologie du Quebec. This was done with fully informed consent of both laboratories.

6) Subjective clinical symptoms were elicited in a standardized way without deviation from the probes and questions used, following a standardized questionnaire administered by trained health services research interviewers. A distinct feature of this project was the "ritualized" medical examination in which the physicians observing and measuring physical signs followed a precisely standardized method and sequence of examination and reporting for all findings. These physicians were only allowed to speak to subjects sufficiently to have them do the clinical manoeuvres required. Thus those physicians' opinions were not invoked about physical findings; only physicians' observations, with the highest attainable rigour of quantification possible, were recorded.

In contrast, by design, the judgemental medical examination was not standardized. The senior physicians involved were allowed to function as they normally would in university clinic practice in order not to restrict their ability to diagnose conditions that may have been missed by the other more inflexible data-gathering procedures. Issues of reproducibility were addressed by having each judgemental physician work in each of the comparison areas as far as was possible. However, the data gathering form employed for the judgemental medical examination was standardized.

7) After the clinical co-principal investigators returned to Montreal, they consulted with other medical specialists to develop formal algorithms to identify specific clinical conditions. These algorithms used data from the questionnaire and ritualized examination as well as from physiological and biochemical tests. The data were extracted and combined by means of computer programs to assure the objectivity and repeatability of counting the frequency of conditions and describing the frequency of clinical phenomena.

8) Comparison of electrocardiograms were based only on the computerized interpretations. Thus, we deliberately traded some degree of validity, which may have been decreased by not taking clinical judgement into account, for the reliability and precision of the computerized ECG measures.

9) Selected descriptive variables from the questionnaire were verified independently by a supervisor. This was achieved by re-interviewing approximately 10% of the households by telephone after the interview had been completed.

10) All data that were not self-coding and which required coding by the field staff or the analysis staff in Montreal were

double coded in a random sample of 10% of the participants. This was to determine an error rate in coding and to make corrections in the process when necessary.

11) All coding and transformation of data followed pre-tested standard techniques recorded in coding manuals created and adapted in the field. These are on file for reference.

12) We employed the usual method of 100% double entry and verification of data at the time of keypunching.

13) All data gathering in the field was completed in one season for the crossectional survey and by mail within an eight month period for outmigrants.

14) Very high response rates were set as the goal initially. The requirements were specified in advance to be at least 90%. We achieved those rates in all three areas within the time period specified in the protocol.

15) The response rates were similar for the three areas in the crossectional survey across the three areas and for the three outmigrant groups.

16) Half of the research team worked in the SR control area in

the first half of August 1985 and moved to the DCCI area after August 15, while the half that had started in DCCI moved to the SR area on August 15. Thus the two areas had approximately equal amounts of information elicited by each half of the staff.

17) For certain data that could have been susceptible to variation due to a change in prevalence of pollens and other allergens between June of 1985 to the end of the summer, a repeat of selected findings was done later in August among respondents who had been first evaluated in June. This was to check on any intra-seasonal variation in the findings of relevance.

18) For similar selected variables related mainly to the respiratory system, clinical and laboratory findings were repeated in winter (late January 1986) to determine whether there was inter-seasonal variation. Again, this focussed largely on respiratory clinical findings and respiratory function in the laboratory.

19) The field staff working in the Index Area did half the determinations in the first half of the winter exercise period then moved to the SR area, while those in the SR area moved to the Index Area in the second half. Thus each team

elicited information in both areas for the winter exercise.

20) In order to determine whether there was bias due to selective migration of persons in and out of the three areas for health reasons, an exhaustive search of outmigrants was done. These were people who had lived in the area at any time after 1957 and had moved out or died since that time.

21) Outmigrants were sought using multiple sources. Reporting by at least two independent sources was required for an outmigrant to be officially counted as part of the denominators.

22) Clinical significance for differences between the areas contrasted for any self-reported dichotomous variable required that the levels of statistical significance and power employed in the analysis be declared in advance.

23) Until near the end of the analysis period, the analysis of data was done with the Principal Investigator and co-principal investigators largely blind to the identity of the comparison groups contrasted. This minimized conscious or unconscious approaches to the data that might have influenced conclusions in any particular direction.

24) During a major part of the summer, eight simulated or standardized patients were examined by the sequence of clinical and para-clinical determinations in the field to determine whether there were any drifts in performance by the data-gathering staff.

25) All editing of outmigrant information was performed without knowledge of subsequent outcomes such as cancer or untoward reproductive events.

26) When discretionary choices were made regarding editing of outmigrant information, the a priori policy was adopted that the estimate giving rise to lower person-years of risk was used, so as to decrease the expected number of cancers. This policy is liberal in that it increases the likelihood of concluding that there was an excess in the Index Area.

27) Lastly, before official submission of the findings to the Scientific Advisory Board of the Acid Deposition Research Program, all findings were submitted for exhaustive criticism by an international panel of epidemiologists, biostatisticians, clinical investigators, and environmental scientists and chemists (the SAG). One specific mandate to them was to search for any bias which the investigators had not suspected that could either be checked or corrected

prior to the public release of the findings.

We would have liked to institute a few more measures to minimize bias and to enhance the reliability of the data. However, in a non-experimental design and with geographic and budgetary constraints this was not possible. For instance, ideally, all participants should have come to an examination and interview centre intermingled from the various areas so that the field staff could be blinded to their group identity. With the areas as wide apart physically as they were, we could only do this partially, affecting less than 100 participants among the three areas. Alternatively, it would have been preferable to have examinations going on simultaneously in the three areas throughout the summer and to have random allocation of subjects to day of examination. Again, this was not feasible. It would have been better not to have families come in clusters, to minimize spurious intra-household correlations in findings. Because it was necessary to do proxy interviews and because of long distance for some of the respondents to travel, it could only be arranged to have most of the families examined in clusters, as families. However, despite these and a few other shortcomings, our methodological results suggest that serious biases were kept to a minimum and that they are unlikely to have any important effect on any of the findings for the major preselected variables of this project.

18.3 Discussion of the Findings Pertaining to the Main Outcomes Put Forward in the Protocol of the Medical Diagnostic Review Project (MDR)

Here we discuss the findings of the study and qualify some interpretations with attention to the protocol, the hypotheses of relevance and the objectives of the MDR.

18.3.1 Mortality

Having used the best available information from the Alberta Bureau of Statistics and from Statistics Canada, complemented by data we have from our own follow-up of outmigrants, we calculated the standardized mortality ratios for the Index Area 1970 cohort. We found that the mortality experience of this cohort in the 15 years from 1970 to 1984 was similar to the experiences of two reference populations, one containing the Stirling/Raymond (SR) area and the other containting the DCCI area. Mortality in the Index Area 1970 cohort was considerably lower than that of the general population of Alberta.

18.3.2 Cancer

With respect to cancer rates, the objective specified in the protocol was to determine whether there was an excess of overall cancer in the Index Area. The data do not suggest any such excess. Secondary analyses, including analysis by certainty, analysis by length of residence in the area, and analysis by location of residence within the area all serve to confirm the general impression that the profile of the overall cancer experience is very similar to that of similar populations in Southern Alberta.

The IA is a rural farming population with a great deal of exposure to the sun, and thus an observed excess of non-melanotic skin cancer was not unexpected though it was also not statistically significant. Such cancers are curable and do not contribute materially to health hazards of individuals or populations. If we exclude non-melanotic skin cancers from the analysis of the Index Area and from the reference populations with which we compared it, we then find a deficit of killing and disabling cancers in the Index Area although the deficit is not statistically significant. An unexpected finding was a small statistically non-significant excess of cancer of the prostate (compared to expected incidence). Such an excess has also been noted in parts of Southern Alberta including Census Divisions 1 and 3 before; it is not unique to the Index Area (Bako, 1982). Other studies have investigated cancer of the prostate in this general region, and to our knowledge no specific risk factors other than ethnic origin, level of education, and reproductive activity have been identified (Hill, 1985).

18.3.3 Special Studies of Trace Metals in Human Tissues

Previous studies have reported elevated levels of certain trace metals among samples of volunteers in Southwestern Alberta. The concern of the population about such findings and their potential impact on health is understandable and continues to be high. The levels of trace metals reported in the present study were similar and very low in all three areas, and more than 93% of all values for all metals were either undetectably low or normal. We took special pains to control for the quality of the laboratory work in our studies of trace metals. Hair samples with certified metal values from the Japanese National Institute of Environmental Studies were measured by both laboratories to verify absolute measurement accuracy. Duplicate specimens were used to check laboratory reproducibility and also to cross-check one laboratory against the other in a blind manner. Data reported in the present study gave evidence of high reliability and validity of the laboratory determinations used to reach our conclusions. Thus, our findings that determinations were either normal or below detectable limits are stated with a great deal of confidence. It deserves special mention that residents of two Hutterite colonies, one within the Index Area and one adjoining the main comparison area in Stirling/Raymond also had values that were normal and similar to one another. Hutterite people tend to consume locally grown food to a greater extent than the non-Hutterites in the IA and SR. Thus, any differences between IA and SR in trace metal values of Hutterites who could be more susceptible to local environmental conditions would have been of enormous importance. However, this did not prove to be the case.

18.3.4 Pulmonary Function

We took a great deal of care to minimize the effect of factors that might introduce false values in any of the individual or aggregate estimates of pulmonary function in this project. Technicians were divided evenly among the areas studied to the maximum extent feasible; early season and late season determinations were done to check for learning and technical biases. As noted elsewhere, winter and summer reassessments showed no appreciable observer variation that could lead to inappropriate conclusions. The seasonality effect of the allergy/hayfever season was checked. Over 90% of the respondents in all areas had pulmonary function tests done and 90% had readings reproducible within 5%. The strongest trend seen was the greater mean FEV_1 in IA children as compared to SR children. In all areas however, FEV_1 was on average of at least 100% of predicted in children.

The principal indicator of pulmonary function we used, namely the FEV_1, was on average at least 100% of predicted for all the areas. As discussed in methodological results the summer reproducibility testing suggested FVC measurements may have been diminished during the month of June as compared to July and August. If present at all, systematic error would have tended to increase the measured FVC in the Index Area as compared to the other three areas and thus not the conclusions of the study.

18.3.5 Reproductive Risks and Outcomes

18.3.5.1 Some Relevant Considerations about the Biology and Epidemiology of Human Reproduction

Adverse reproductive outcomes caused by a previously unrecognized environmental risk factor may present as part or all of a spectrum of effects. This spectrum includes infertility, abortions (miscarriages) early or late in pregnancy, stillbirths, prematurity/low birth weight, neonatal deaths, birth defects (congenital anomalies) and delayed or inadequate childhood development.

Many adverse fetal outcomes, whose causes are largely unknown, occur in all parts of Canada and elsewhere at "background" rates that are fairly well established.

To determine the possible effects of an additional environmental agent, one must establish that rates of occurrence of adverse reproductive effects are significantly greater than the common "background" levels. In addition to these "background" levels, some known causes of certain adverse reproductive outcomes can confound the analyses. These include smoking, use of alcoholic beverages or other drugs (such as thalidomide), infections (such as rubella), and maternal malnutrition during pregnancy. Part of the incidence of birth defects is due to genetic predisposition within families. Maternal age is correlated positively with certain adverse outcomes.

A noxious chemical agent causing fetal loss or birth defects is most commonly a teratogen that produces changes in embryonic development incompatible with fetal survival, a toxic agent that kills the embryo or fetus, or stimulates premature expulsion of the product of conception. One would expect fetal losses to be relatively much more frequent than surviving children with birth defects in the presence of such noxious chemical agents.

18.3.5.2 Risks

It is not known what specific substances associated with sour gas, if any, should be regarded as suspect teratogenic risks: is it the inorganic acids, the volatile hydrocarbons, the sulfur and heavy metals, or some combination of these and other substances?

There is evidence suggesting that sea water contaminated with petroleum in quantities insufficient to kill marine life retards reproduction (Schultz, et al. 1982). Non-radioactive heavy metals, sulfur and the inorganic acids of sulfur and nitrogen oxides have not been previously implicated specifically in reproductive abnormalities in dosages insufficient to cause ill effects in other human organ systems. From the medical history and medical examination data in the other parts of this Alberta study, there is no evidence of deleterious effects on other organ systems in which adverse outcomes might show up sooner than in the time span of a human generation. Also, the low levels of heavy metals found in the vast majority of those examined suggest that these are not likely to be causes of reproductive abnormalities. It is known that certain aromatic (ring type) hydrocarbons, especially with nitrogen linkages, are both embryotoxic and teratogenic (Guerin, et al. 1981). However, it is believed that the hydrocarbons in this Alberta study are aliphatic (long chain) rather than aromatic.

It is not known what "dosages" of potential noxious agents have been released by the industries involved, or received by the populations exposed to them, now or over the years, with the exception of the heavy metals in the clinical studies mentioned above. These heavy metal studies suggest a virtual absence of exposure above that expected in a rural non-industrial environment. Presumably the volume and nature of the emissions varied from time to time, and their geographic distribution also varied with wind direction, velocity, and other climatic conditions including possible atmospheric inversions.

If from the above analysis, it is hypothesized that, in the MDR, one is faced with exposure to some harmful agent not previously recognized as causing adverse reproductive outcomes, then the probable mechanism of action of the supposed harmful substance is also unknown. Clues to such a mechanism could be found in the type and gestational timing of birth defects or the frequency of chromosomal abnormalities or new mutations that might be excessive in the exposed population in contrast to one not exposed. However, no such excess has been found.

One is left therefore with three observations:

1) An exposed population in which the community perception of adverse reproductive effects is present;

2) A study in which no significant excess of adverse reproductive effects could be demonstrated in the "exposed", in contrast to the "not exposed", populations;

3) No data from which to develop and test a hypothesis that some harmful agent may have been present, which was undetected by this historical study, but which might be detected by a large prospective study or by using animal models.

In discussing the many methodological pitfalls in such studies, world renowned authorities on birth defects described two that are particularly relevant to the MDR study.

1) A woman's recall of an early pregnancy loss--which may be difficult to distinguish from a late or missed menstrual period--and her recall of a birth defect in a miscarriage--is likely to be greater if she knows she has been exposed to some possibly toxic substance "...especially one which has

received a good deal of publicity" (Hook, et al. 1980). The vast majority of reproductive losses occur so early in pregnancy that there will rarely be a hospital record or vital statistics report to confirm the mother's recall; even if so confirmed, those mothers who fear effects of an adverse exposure (such as sour gas emissions) are more likely than non-exposed mothers to seek the hospital care that leads to such confirmatory records. This leads to a "positive bias" in comparisons of "exposed" and "not exposed" populations.

Therefore, in this retrospective Alberta Reproductive Risks and Outcomes Study, based largely on women's recall of their reproductive histories, one might have anticipated higher rates of reported reproductive loss in the "exposed" women in the Index Area than in the control area "not exposed" women. In fact, no such difference was found.

2) "...it is always conceivable that some factor that appears to be associated positively with embryonic and fetal death is instead fetoprotective and acts by postponing the time of death from an earlier stage of gestation when such an event would be less likely to be recognized, to a later stage." Thus "...it may be in fact impossible to distinguish, at least by 'retrospective' or historical studies, whether an

> agent or biological factor is associated with diagnosed embryonic and/or fetal death because it tends to delay the event to a time when recognition is more likely, or whether it is in fact embryotoxic." (Hook, et al. 1980.)

One needs the concept of a "critical time" when the suspected agent is likely to have its adverse effect, independent evidence that such substances do have such an effect on cell division, and evidence on the extent of the exposure during the "critical time", to try to address this issue. Such information is not available for sour gas.

18.3.5.3 Interpretation of Findings

It is very difficult to measure and evaluate the potential influence of occupational and environmental exposures on reproductive health. There are two main reasons for this. One is that the influence of adverse exposures can take many forms. Physiological mechanisms can be disturbed. There may be mutagenic effects on gametic cells. There may be an increase in cytogenetic abnormalities, or there may be teratogenic effects. The second factor is that these effects might result in many different kinds of potential abnormal outcomes. There may be primary or secondary infertility, an excess of early or late fetal loss or an increase in the incidence of birth defects.

Other factors that must be considered include genetic differences in the susceptibility of individuals to environmental agents, the potentially subtle nature of many environmental effects, and the high background frequency of adverse reproductive outcomes.

Background rates of abnormal reproductive outcomes are certainly high, with figures usually quoted in a range of 10% to 15% of couples for infertility, 15% for early spontaneous loss and 1% to 8% for major congenital anomalies. The variation in figures is because of differences in definitions of numerators and denominators, length of surveillance, and methods of ascertainment. Thus the scope of the methodological challenges is vast. (Kline, et al. 1984.)

The difficulties in accurately assessing risks are also compounded in any study by additional problems such as small sample size, difficulties in quantifying exposure dosage, changes in reproductive patterns with time, differential recollection of reproductive events, potential biases associated with heightened awareness of environmental exposures, and the difficulties of validating data medically, especially fetal losses. Also there are many confounding factors to be considered, such as the use of alcohol and tobacco, family history, earlier reproductive history, and maternal age.

The limitations of this type of study clearly apply to the Alberta project, especially with respect to small sample size and the unavailability of validated data on reproductive outcomes. Given these serious limitations it is encouraging to note that self-reported rates for spontaneous fetal loss and for major congential anomalies at birth in the Index Area do not exceed those expected on a population basis despite the potential for heightened recall in IA and DCCI areas. In addition, the rates are not materially different from those in the comparison regions. The rate of miscarriage in very young women (less than 20 years old) in the Index Area is slightly but not statistically significantly increased, but the figures for the comparison areas indicate possible underascertainment. Conversely, the results could simply be due to instability of reported rates in small sample sizes. The physical examinations on the participants born in any of the areas indicate malformation rates of 1% to 2%. As expected, these figures are lower than birth prevalence rates as many children with major malformations die in infancy. In addition, some common genetic disorders of adult life, such as polycystic kidney disease, would not be influenced by environmental factors.

Having made comparisons of incidence and prevalence of phenomena related to the reproductive process and outcomes of reproduction in six categories, we have found no differences that are clinically significant in any of those categories. The evaluation included assessment of fetal loss, comparisons of prematurity and low birth weight, comparisons of rates of birth defects by definitions agreed upon before the analysis was done, comparisons of fertility, comparisons of fecundity, and comparisons of childhood development. Careful attention was given to relate exposure and outcomes in an environmentally and clinically meaningful way. Thus, in both the summer crossectional survey and the follow-up of outmigrants, women-years at risk were derived as denominators so that that differences, if any, would be correctly attributed. We tried to minimize bias in data-gathering and we have every reason to believe from determinations of the quality of our data that if bias exists, it influences all groups under comparison in a similar manner. Our absolute rates might be incorrect (on the low side) but any systematic error is expected to operate in the same direction and magnitude for all areas. Thus, the relativity of the findings among areas is valid.

18.3.6 Health Status

Thus far we have discussed mortality, cancer incidence, trace metal levels in hair and blood, pulmonary function, and reproductive risks and outcomes amongst residents of the Index Area. While these are reliable indicators of some aspects of the health of the population involved, many specific points among these variables are not sensitive to the low-dose exposures that residents of this area may have experienced. For that reason, the MDR included a comprehensive array of additional measures: (i) residents' perceptions about their health; (ii) perceptions about their exposures to risk factors such as environmental pollutants; (iii) their self-reported symptoms, disabilities, and diagnoses; and (iv) self-reports about their use of health professionals and health facilities. We also evaluated clinical findings as observed by specially trained physicians and senior university consultants. Such data may be affected by the perceptions and feelings of residents of these areas. For this reason, we collated and corroborated symptoms, signs, physician findings, and laboratory tests in various relevant categories. As described earlier in the Methods Section, this study took special care to standardize data concerning physical findings by utilizing a "ritualized" medical examination, standardized for every participant in the study regardless of the area of residence.

Prior to entering into the discussion of each group of health status parameters, we raise several cautions regarding the interpretation of these data. First, it must be recognized that self-reported perceptions regarding health, symptoms, and disability may be influenced by factors extraneous to actual health status. In particular, heightened concern about health may lead to a heightened awareness of symptoms and taper to higher use of medical resources. Second, we must point out that literally hundreds of comparisons were made among these areas and the possibility of chance associations in such a complex analysis must be taken into account. For this reason, the primary focus must be on those variables which were specified as cardinal prior to the analysis; results of analyses regarding other variables may be important but they can be used only as hypothesis-generating information. Third, pre-specified criteria for clinically significant differences were set out prior to the conduct and analysis of this study. These levels of clinical significance were based on prior clinical judgement and experience with the variables being studied as well as on *a priori* power calculations. Such calculations indicate that lower differences would not be detectable with adequate power given the population of the Index Area as demarcated for us by Alberta Environment. While the levels set for clinical significance are arbitrary and it may be argued by some that the levels we used are too high or too low, these levels were approved in advance by the expert peers of the Scientific Advisory Board. Furthermore, all raw data are clearly displayed or available on request; any reader who wishes to choose a different level of clinical significance may, with scientifically admissible justification, do so and interpret the data accordingly. It is also important to point out that once *a priori* clinically significant difference levels are published and approved, then they must be upheld throughout the formal hypothesis testing. Accordingly, for any variable that fails to attain a difference greater than or equal to the pre-set level of clinical significance, the null hypothesis cannot be rejected; in such cases, the proper conclusion is that the study failed to detect a difference between the groups contrasted.

Another important point to be raised concerns the interpretation of the ancillary comparisons between DCCI and SR-M. As noted in the Methods Section, the primary comparison in this study involves the contrast between the exposed IA and the unexposed SR control area. However, if any adverse effect on the IA population detected in such contrasts is eventually to be attributed to exposure to sour gas emissions, then it is reasonable to expect analogous adverse effects, similar in both magnitude and direction, in the corresponding ancillary contrast between the exposed DCCI sample and the unexposed SR-M sample. When an adverse effect is detected in the IA vs. SR comparison, whether clinically significant or not, and it is mirrored in the DCCI vs. SR-M comparison, we referred to it as "corroborated". When the analogous relationship in the DCCI vs. SR-M contrast either fails to hold or is reversed, we used the term "uncorroborated".

18.3.6.1 Indicators of Disability

The study included an assessment of whether participants in the Index Area are more or less disabled than residents of the control area in Stirling/Raymond. Among adults, we concentrated on prevalence findings, namely the status of the respondents in the two weeks prior to the standardized interview. We measured loss of physical activity. bed disability, days of activity lost per person during the preceding two weeks, and days per person spent in bed for the preceding two weeks. The number of persons who had had any disability was of special interest. We then calculated the average number of days per person in which disability was experienced among those who had suffered any loss. Having noted that approximately 80% of the adult population in both the IA and the SR area are free of any loss of activity and that approximately 92% in each area are free of bed disability, there is a slight trend of 3.9% greater activity loss in the IA than SR. Conversely, the number of days per person spent in bed in the prior two weeks is slightly higher for the SR than the IA. For the other three tables concerning disability among adults, there are no important differences.

In the disability group of variables, the differences between IA and SR, whether they pointed in one direction or another, were not corroborated by the ancillary comparisons of DCCI vs. SR-M.

18.3.6.2 Utilization of Health Care Resources

Four measures of use of health care were assessed to explore the different rates of demand for care in the Index Area and the comparison populations. There were no important differences among the four categories of utilization measured. The recall spans were selected with attention to demonstrated validity ranging from one-year recall for hospitalization to two weeks for encounters with health professionals to two days recall for the use of medications. No differences were observed in use of medications for compounds prescribed by a medical doctor, while medications without advice of a medical doctor were taken appreciably more frequently in the IA than in SR, a finding corroborated by similar rates for medications without prescription noted in DCCI compared to SR-M. Both encounters with health professionals and use of health facilities were similar to rates reported for other parts of the country. There is no suggestion that Southern Albertans are unique in this regard.

18.3.6.3 Prevalence of Chronic Self-Reported Irreversible Disease

There was no difference between IA and SR in the self-reported point prevalence of any of the chronic irreversible diseases among adults explored except for the prevalence of musculoskeletal ailments of the joints and limbs. Hips and legs were affected primarily; other joints and limbs had similar rates. There were no differences for back pain. Although the difference in musculoskeletal disorders was corroborated by comparisons of DCCI vs. SR-M, we had not hypothesized musculoskeletal disorders as a cardinal problem in advance.

18.3.6.4 Spontaneously Reported Health Problems

Without probes or suggestions made to the respondents, one of the first questions in the standardized data gathering instrument (Question 2A) concerned any health problem that might have occurred in the preceding two weeks. We consider such spontaneously reported health problems to be of clinical and epidemiological importance, especially when elicited early in the data gathering process with each subject. Among adults, the prevalence of spontaneously reported health problems was slightly higher in IA than in SR. This was not corroborated in the contrast of DCCI vs. SR-M. Among children there was no important difference.

18.3.6.5 Paraclinical Laboratory Investigation

Among adults and children over seven years of age the findings of urinalyses and the findings concerning biochemical abnormalities showed no important differences between IA and SR. The proportion of persons with selected clinically important ECG abnormalities in each area showed no difference either.

18.3.6.6 Diagnoses Made in Medical Judgementals and Consultations

In different analyses done somewhat differently for different purposes, approximately 5% more people in the SR were considered ostensibly healthy than in IA. Rates of diagnoses grouped in broad disease categories resulted in somewhat higher rates for the respiratory system, the circulatory system, and the nervous system among IA residents. Findings for the circulatory system were corroborated in the DCCI vs. SR-M comparison. However, five other groupings, including the prevalence of the most common diagnoses taken together, showed no differences. With the exception of "hypertension with complications" and "chronic bronchitis", delineation or diagnoses using formal algorithms showed little difference for most of the important diseases explored. The differences for those two conditions, namely hypertension with complications and chronic bronchitis technically do not attain clinical significance by our pre-set criteria. However, the differences are sufficiently high for the investigators to "tag" them as worthy of attention in the balance of the analysis. We also noted that rates of musculo-skeletal ailments were somewhat higher among residents of IA than SR. Again, technically, this difference was not clinically significant but worthy of attention. (See section focussing on specific disorders.)

Results of the study of period prevalence of reported illnesses from 1970 to 1985 for the 1970 cohorts of the Index Area and the Stirling/Raymond area militate strongly against bias due to selective migration related to health. The differences in hypertension are of the same magnitude and direction as for the crossectional findings in the 1985 cohort. Also, the differences and direction for chronic bronchitis incorporating self-reported data from outmigrants are similar to the crossectional contrasts. Similarly, the yearly incidence density of reported respiratory diseases suggests that the crossectional findings have not been biased by selective migration.

18.3.6.7 Seasonal Influence of the Relationship Between Health and Place of Residence

Observed differences in measured variables between summer and winter could be due to changes in climate, interviewers, physician examiners, spirometry technicians, and/or spirometers used. The winter reassessment was done not to determine whether there were summer or winter differences but to determine whether or not the relationship between health and place of residence was influenced by season. For example, it was not important to know whether or not the prevalence of hay fever decreased during the winter months but rather whether or not differences in health between IA and SR could be found during the winter that were not apparent in the summer. To answer this question summer/winter differences in IA were compared to summer/winter differences in SR. (This is equivalent to comparing IA/SR differences in summer with those in winter.) For both areas combined there were increases during the winter in spontaneously reported health problems and in symptoms of cough and phlegm. There were non-systematic changes in physical signs and small systematic reductions in pulmonary function measurements. Comparing summer/winter differences in IA to summer/winter differences in SR revealed small differences with no systematic trends towards one area showing greater differences than the other area. In summary, the winter reassessment did not demonstrate any influence of season on the relationship between health and environment.

18.3.6.8 Cardinal Clinical Findings

By far the most important assessment within the group of variables designated "health status measurements" concern the cardinal clinical variables. These are medically ascertainable health findings that were established in advance as plausibly associated with the risk factors of interest among people exposed to sour gas. We summarize these findings here, progressing from subjective symptoms, to objectively observed signs by physicians, to diagnoses based on both symptoms and signs.

Starting with subjective cardinal symptoms, both adults and children in IA exhibit higher rates of cardinal symptoms in the majority of individual variables than do adults and children in SR. When we assess prevalence by taking into account the percentage of people who had at least one probed cardinal symptom, the rates are higher for adults but not for children. The higher rates for adults are not corroborated in the DCCI vs. SR-M comparison. In contrast, the prevalence of objective cardinal signs is lower in IA than in SR, whether one considers them combined or as individual cardinal signs. These lower rates in the exposed IA participants are corroborated by lower rates of cardinal signs in DCCI compared to SR-M.

The prevalences of cardinal diagnoses are essentially equal in all areas.

As shown in detail in earlier chapters, there is a recurring pattern of higher frequencies or higher prevalences of symptoms, health related events, and diagnoses in the Index Area than in SR. While none of these differences taken individually are large and none of them are clinically significant, the observed pattern requires some comment. We believe that this pattern of small and non-significant differences does not indicate a collection of serious but individually undetectable threats to health. First, there is a large number of such entities, and they are not all plausibly associated with the environmental risk factor of interest. Second, they are not always biologically and plausibly related with one another. Third, the same direction or magnitude of difference is not consistently corroborated in DCCI (exposed) versus SR-M (unexposed). Fourth, the presence of symptoms or other subjective perceptions is often not confirmed by more objective data, such as clinical signs and especially not by laboratory findings. Fifth, there is a distinct pattern of decreasing differences between IA and SR as one progresses from clinical findings with a large subjective component to those in which there is greater dependence on objective findings. Lastly, where we have outcome determinations of "hard" variables such as confirmed incidence of definite disease and mortality, we have not shown an excess of either important diseases, such as cancer, or events, such as death.

We are left with one of two choices: either we impute all the unrelated and mostly uncorrobated events to emissions of sour gas in the IA area; or we attribute this pattern of small and nonsignficant differences, especially in subjective elements, to a combination of selective recall in a sensitized population, perhaps combined with an undetectable detection bias on the part of examining physicians who could not be blinded to the group membership of the participants.

18.3.6.9 Additional Health Status Indicators

We found no difference in symptoms that reflect mental health status. The IA area is near the top of the "healthy" end of the scale and is similar to all other areas. A considerably higher proportion of IA residents than of SR residents responded "Yes" to questions about factors that they thought might affect their health. In contrast, the residents in DCCI were similar to SR-M with respect to this variable. For the objective assessment of visual acuity done by a standardized technique in the laboratories of the project, the findings were essentially identical for IA compared to SR and also for DCCI compared to SR-M.

18.3.6.10 Focus on Selected Diagnoses, Signs and Symptoms

In this section we highlight some of the data pertaining to selected diagnoses, signs, and symptoms. Certain comparisons illuminate the differences between findings for self-reported phenomena and those corroborated by a ritualized examination or subsequent judgemental and consultation visits. For example, in Table 13.3/1 we note approximately a 5% excess in the prevalence of persons in the Index Area reporting eyesight problems not corrected by glasses. Similarly, in Table 13.4.2.1/1, the prevalence of adults reporting itching, burning, or watering of the eyes in the preceding two-week period was approximately 6% higher in IA than in SR. This excess in the reporting of ocular symptoms contributed to the increased prevalence of the diagnosis of probable ocular conjunctivitis amongst IA residents when derived using the computer-assisted algorithm (see Table 13.4.1.3/2). However, the reporting of ocular symptoms was taken into account in the algorithm which generated the diagnosis of conjunctivitis, and these self-reported symptoms were not coherent with more objective criteria of professional observation. In particular, red eyes were detected during the ritualized medical examination more often in SR than in IA (see Table 13.4.2.1/5). Moreover, visual acuity tests showed no evidence of important differences in the prevalence of visual impairment across the four areas. Finally, the frequency of diagnosis of conjunctivitis by medical judgmental examination was similar in IA (2.5%) and SR (2.1%) (see Table 13.4.1.3/1). This example illustrates the frequently encountered discrepancy in survey research, when self-reported data overestimate the frequency of diagnostics of the same condition by a physician examining the same subject at the same time.

Another example is that the rate of birth defects reported by participants and outmigrants (Table 16.4/2) was 6.3% in IA and 4.6% in SR, but the rates of medically-observed congenital anomalies were reversed, to 1.99% for IA and 3.3% for SR (Table 16.4/1).

A further example of this reversal is seen in the data pertaining to the developmental characteristics of children (Tables 16.5/1 and 16.5/2). IA parents reported about 10% more developmental delay in their infant sons than SR parents. Similarly, about 9% fewer IA parents than SR parents reported that they were very satisfied with the development of their infant sons while about 5% less of IA parents than SR parents reported that they were very satisfied with the development of their infant girls. When we attempted to corroborate these findings concerning developmental delay in children with more objective evidence, we were unable to substantiate the presence of any differences.

Specifically, we detected no differences between IA and SR children with regard to height, weight, performance on the Denver Developmental Screening Test, or the prevalence of delayed sexual maturity according to clinical findings (Table 16.5/2).

As pointed out earlier in this discussion section, we singled out "hypertension", and particularly "hypertension with complications" as worthy of special attention (Table 13.4.1.3/2). We then reanalyzed the data as if the entire MDR project had been done to do screening for hypertension. The most significant objective finding was that the mean diastolic blood pressure for adults over 25 was 79.5 mmHg in IA and 80.3 mmHg in SA. We established that this comparison was not influenced by different medication practices between IA and SR: among those reporting high blood pressure, 75% of those in IA reported currently taking heart or blood pressure medication as compared to 73% in SR. (The mean diastolic blood pressure in DCCI was 78.9 mmHg and 80.8 mmHg in SR-M, with 72% and 70% respectively of those with hypertension currently taking medication.) However, 3% more participants reported hypertension in IA as compared to SR (X% vs. Y%), and 6% more people in IA as compared to SR stated that they have or have had physician diagnosed hypertension (X% vs. Y%). With respect to hypertension-related paraclinical findings, IA as compared to SR showed the following minimal differences: 1% more with proteinuria, 1.5% more will serum urea elevations, 1.1% more with ECG evidence of ventricular hypertrophy, and 0.7% more with ECG evidence of myocardial infarction. In contrast, the diagnoses done with formal algorithms yielded a 3% difference in hypertension in IA, higher than SR, based on subjective reporting and objective blood pressure measurements. Since the objective measures were similar in the two areas, this 3% difference could only be due to the difference in subjective reporting. Thus, although IA reported more hypertension than SR, the ultimate criteria for population problems with hypertension is the mean level of blood pressure, which was slightly lower in IA than in to SR; and differences in related paraclinical findings were small.

IA had a 4% higher rate of chronic bronchitis than did SR. The algorithm for this diagnosis used subjective reporting of mucus hypersecretion exclusively and was not concerned with impaired respiratory function. In the present study, we have been able to show the strong relation between cigarette smoking and self-reports of sputum production; 10% in non-smokers as compared to 29% in current smokers. It is therefore inconsistent that in DCCI, with a higher percentage of smokers and more exposure to sour gas emissions, the proportion with chronic bronchitis was 0.5% lower than in IA. Contrary to the findings from questionnaire and computer algorithms, chronic bronchitis was diagnosed by judgemental physicians less frequently in IA than in either SR or DCCI. These physicians on site reported the difficulty of confirming chronic bronchitis as elicited by questionnaire. Participants often did not distinguish upper from lower respiratory tract secretions. Although this may have increased the reported prevalence, it was not expected to bias the between-area comparisons. Chronic bronchitis is a non-specific response of the airways to irritation and consequently has a multifactorial etiology. Thus, in the present study, the relative importance of cigarette smoking, environmental irritants, and occupational (farming) dust exposures could not be easily discerned.

Most of the apparent excess of symptoms and conditions related to the musculo-skeletal system was in self-reported findings regarding legs and hips. Complaints regarding all other joints and extremities were similar among areas. There was no excess in men as compared to women and only a slight increase in older as compared to younger people. We are unaware of any clinically plausible mechanism that might explain this, and musculo-skeletal disorder symptoms and signs were not cardinal in our proposal. Therefore, this finding may have resulted either from multiple comparisons as a statistical artifact or selective recall on the part of participants.

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19. CONCLUSIONS

19.1 Mortality

We conclude that the mortality experience of the Index Area from 1970 through 1984 is that which would be expected based on reference rates from similar populations in Southern Alberta and considerably more favourable than for Alberta as a whole.

19.2 Cancer

We conclude that there is no evidence to suggest an excess in the overall incidence of cancer in the Index Area.

The primary objective of this component of the study, as set out in May of 1985, was to investigate whether the overall incidence of cancer among residents of the Index Area was higher than what should be anticipated from cancer rates in sociodemographically similar populations. Using the Index Area 1970 cohort as our study population and using 3 prespecified reference populations from rural areas in Southern Alberta, we have been unable to detect an increase in the overall incidence of cancer in the Index Area above that which is expected. Based on these data and based on the pre-existing evidence (see section

6.1.2), which includes 2 previous studies that failed to detect any elevation in this area in cancer incidence rates, in physician visits for neoplasms, or hospital days for neoplasms, we conclude that there is no detectable relationship between the overall incidence of clinically serious cancers and residence in that area of Southwestern Alberta known as the Index Area. We did detect a small and statistically non-significant excess in the incidence of non-melanotic skin cancers, but if this is not a chance observation it may be due to the fact that this area of Alberta receives the highest annual amount of net solar radiation in Alberta (Hydrologic Atlas of Canada, Environment Canada, 1976) and its population, with a high proportion of farmers and ranchers, may thus experience an increased exposure to the sun. In any case, these lesions rarely lead to any appreciable morbidity or mortality. The data suggest that residents of this area experience a lower than expected overall incidence of the remaining killing and disabling malignancies.

19.3 Levels of Trace Metals in Hair and Blood

We conclude that levels of trace metals in hair and blood specimens from people in the Index Area are within normal limits and are not different than those found in specimens taken from similar populations assessed in this study.

19.4 Respiratory Function

We conclude that the distribution of respiratory function of residents of the Index Area is within normal limits and similar to the respiratory function of residents in the reference populations.

19.5 Reproductive Risks and Outcomes

We conclude that the prevalence of medically-observed birth defects in the participants of the crossectional survey was similar in all areas. The observed rates of the more common major birth defects are similar to the expected rates derived using Manitoba registry information applied to the Southern Alberta population.

The cohort under assessment in the Index Area was small and thus did not yield sufficient pregnancies for powerful statistical analyses. In the absence of a Registry of Birth Defects for all Alberta, the architecture, the tactics, and the timeline of this study permitted only historical ascertainments of reproductive outcomes using medically unvalidated self-reports of participants and outmigrants to derive incidence rates. Within the framework of such unavoidable limitations, the patterns of reproductive events reported to us do not suggest an excess of adverse outcomes. Moreover, the overall rates of fetal loss and birth defects determined in this study do not exceed expected rates derived in other Canadian and North American jurisdictions under surveillance with registries.

Both men and women report slightly higher rates of problems of fertility in the IA compared to the SR area. The differences do not suggest the existence of a health problem in any area we surveyed.

Based on objective clinical assessment, we found no excess of delayed or abnormal childhood development among residents of the Index Area and their offspring.

19.6 Health Status

19.6.1 Health Status Measures and Indicators

From the full array of major health status outcome measurements and indicators we conclude that Index Area residents do not have different prevalences of life-threatening disorders or seriously disabling disease than the SR area.

19.6.2 Objective Cardinal Signs

We conclude that there are no detectable differences between the rate of objective cardinal signs in the Index Area and the rate in the main reference population.

19.6.3 Cardinal Symptoms and Other Findings Reported by Participants

We detected a small excess of some of the symptoms which residents of IA have reported for many years. These are largely the cardinal symptoms. We ascertained heterogeneous complaints which suggest discomfort and sustained distress. The symptoms include burning and watering of eyes, runny nose, itching of the skin, throat irritation, sputum production, tingling and trembling of hands, fatigue, back pain, and leg and hip pain.

19.6.3.1 Interpretation of Differences in Rates of Symptoms and Reported Findings

We conclude that the differences in the clinical entities recollected and reported by the participants which are systematically higher in IA as compared to SR are not large enough to contradict or cast doubt upon the major outcome findings. The differences do not constitute an important demonstrated health effect, either good or bad, when the rates of the subjective events are somewhat higher or lower in IA than in the reference populations.

In a population that has been alarmed for more than two decades about the possible adverse effects of environmental contaminants, it is not surprising that individual persons may often emphasize their subjective sensations, and that such sensations may be reported at a rate higher than can be confirmed with objective evidence. The reassurance provided by the objective evidence may be helpful to many individuals in the IA region.

19.7 Outmigrants

We conclude that persons migrating out of all three areas tend to be younger and somewhat healthier than those that remain in the geographic areas demarcated for the study. Moreover, we did not find differences in the patterns of either reported illness or health related events among the three groups of outmigrants. We conclude further that the percentage of persons migrating due to health reasons is extremely low, similar among the three areas, and unlikely to have resulted in selective migration that could render invalid the cross-sectional comparisons of the populations living in the Index Area, SR and DCCI in 1985.

19.8 Ascertainment of Intraseasonal and Interseasonal Variation

We conclude that the findings of this study were not biased by either intraseasonal or interseasonal variation.

19.9 Association and Causation

19.9.1 Association

We conclude that there is no detectable association between residence in the Index Area (including Twin Butte, Glenwood, Mountain View, Hill Spring and Willow Creek) and levels of measurable health among people who live there now or lived there in the past. Neither is there any suggestion of association between residence in the Didsbury, Carstairs, Crossfield, Irricana area and the health status of the population living there.

19.10 The Health of Residents of the Didsbury, Carstairs, Crossfield, Irricana (DCCI) Area

We conclude that the frequencies of health-related phenomena we measured, including mortality, cancer incidence, abnormalities of reproduction, disease prevalence, levels of cardinal clinical findings, and laboratory tests in DCCI are consistent with the profile of a healthy community with patterns of health indicators similar to those elsewhere in Canada. Most particularly, DCCI is similar in health status to its best-matched reference population (SR-M). These findings are noteworthy because both DCCI and SR-M are sociodemographically representative of people living in rural areas throughout Alberta.

19.11 Pursuit of Causality

We conclude that there is no clinical, epidemiologic, or statistical reason to evaluate the causal significance of any possible association between residence in the Index Area and compromised health since such an association was not detected. The present study was not designed to determine causation of any effect that might have been observed, but our findings taken on the whole do not suggest that there is any causal effect to be investigated.

19.12 Overall Conclusion

The greatest concerns of the population in the Index Area were about excess mortality, high rates of cancer, diminished respiratory function, dangerous levels of trace metals in the body, higher rates of unfavourable reproductive outcomes and birth defects, and delayed or abnormal childhood development. For all the foregoing concerns we have not detected objective evidence to perpetuate the concerns. We are confident of the scientific basis of that reassurance. With respect to symptoms or how people feel concerning possible contamination of their environment, there is a small difference suggesting greater concern and more awareness of one's health and one's sensations among residents in the Index Area. That is entirely understandable and indeed expected given a quarter century of equivocal information about health in relation to the immediate environment which has been diffused in Southern Alberta.

20. RECOMMENDATIONS

20.1 Emission Controls

None of the findings in this study can or should be interpreted as a medical or epidemiological justification to relax continuing efforts of industry and government in the control of potentially hazardous constituents of sour gas emissions and other environmental contaminants. We recommend a sustained policy of strict protection of the environment in Alberta, both in the near term and as a socially responsible long-range plan.

20.2 An Alberta Registry of Birth Defects

To permit valid and reasonably efficient population surveillance or special studies of adverse health events related to reproduction, we recommend that the Province of Alberta promote and fund the upgrading of registration of birth defects. The quality of the resulting Registry of Birth Defects would be similar to the commendable level of quality of the Alberta Cancer Registry. The key principles of operation should be mandatory reporting and active surveillance of exposure factors. Its scope should be province-wide. Its system should facilitate interprovincial comparisons. The initial steps already taken by the University of Calgary in the southern areas of the province should be supported and expanded, with participation of the University of Alberta for full inclusion of northern regions.

20.3 Further Population Health Studies

Any health study in the Index Area will be affected both by the unavoidably low statistical power for detecting small differences or large proportionate differences in uncommon findings, and selective recall of symptoms or health events. This is inherent in the size of the Index Area population and in the nature of the clinical problems and not resolvable by another study and less so by uninformed "private" impressions. We recommend that further clinical, epidemiologic or demographic studies involving new data collection on the field not be done.

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APPENDIX I

SUPPLEMENTARY DETAILED METHODS
AND
SELECTED RESULTS

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Appendix 1.1

REQUEST FOR PROPOSAL

Acid
Deposition
Research Program

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REQUEST FOR PROPOSALS

FOR

MEDICAL DIAGNOSTIC REVIEW PROJECT, ACID DEPOSITION RESEARCH PROGRAM

DECEMBER 5, 1984

Alberta Petroleum
Industry Government
Environmental Committee

1500, 633 Sixth Avenue S.W., Calgary, Alberta T2P 2Y5 Telephone (403) 269-6721

I. Acid Deposition Research Program: An Introduction

The potential adverse impact of acid-forming emission is one of the most significant environmental problems to be encountered in North America in the last two decades. Apart from proven effects on the environment, considerable research is to be initiated regarding the potential effects that these emissions may have on the health of humans, either directly through absorption and inhalation of the emissions or indirectly through ingestion of food and water.

In Alberta, the development of sulphur-containing natural resources results in the release of acid-forming emissions (eg. SO^x, NO^x, H_2S) and other associated compounds (eg. metal particulates, organics). The concern that these emissions may affect the health of Alberta citizens in the Twin Butte area has been the topic of considerable discussion over the last twenty years, particularly in relation to the development of the sour gas industry. Numerous studies and public hearings have been conducted and several reports with attendant recommendations exist to try to resolve this issue. Despite these efforts, it is still unclear whether a direct cause-effect relationship exists between exposure to these emissions and reported health complaints and what role, if any, numerous confounding variables such as lifestyle may play in this problem.

In response to the continuing concern and efforts of many individuals within Government, industry and the public sectors to resolve this question, the Alberta Government and a consortium of industries created jointly the Acid Deposition Research Program (ADRP) to:

- develop a comprehensive understanding of the effects of acid-forming emissions on the environment.
- provide a scientific basis for sound long-term environmental management and regulatory control of these emissions.
- disseminate such information among members, to the public and to government bodies.
- undertake any research deemed appropriate.

In order to achieve these objectives it was recognized that high quality research was essential in both the biophysical and human health areas. Furthermore, it was recognized that this research should be integrated as much as possible to provide more complete answers to key environmental questions. To this end the Members Committee of ADRP established two technical sub-committees to develop appropriate research strategies in the human health and biophysical areas.

The Biophysical Technical Research Committee held a workshop in September 1983, the report and recommendations of which have been submitted to the Members Committee, ADRP.

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The Human Health Workshop was organized and conducted by the Human Health Committee (ADRP) in Banff, Alberta, January 22 to 27, 1984. A report and recommendations was also submitted to the Members Committee, ADRP.

At the Banff workshop there were twenty-three internationally-renowned experts from over seventeen areas of medical and toxicological expertise. Their main conclusion with respect to the current project was that a comprehensive medical diagnostic review was necessary in the study area in order to determine the nature and magnitude of long-standing health complaints which residents ascribe to the emissions of sour gas plants. This conclusion was prompted by the lack of valid data at this time for even a preliminary understanding of cause-effect relationships. Their conclusion was also based on the premise that complaints of health problems from the public are a valid starting point in determining cause-effect relationships.

II. The Medical Diagnostic Review Project: Background

Residents in the study area have been complaining for several years about health problems ranging from dire consequences (eg. cancer, increased mortality, adverse pregnancy outcomes, etc.) to less serious chronic problems such as increased allergies, skin rashes, sore throats, headaches, lethargy, eye irritation, respiratory tract infections, etc. Domestic animals have also been reported to be affected to varying degrees.

Although some attempts have been made in the study area to elucidate the underlying cause(s) of these problems all have fallen short of being scientifically or publicly acceptable. Due to the inconclusive nature of the studies done to date, the residents do not know whom or what to believe. Many residents feel frustrated and overstudied yet still greatly concerned about the risk to their health.

Given this state of affairs and the local sensitivity of the issue, a science advisory body (SAB) of independent outside experts has been appointed to oversee all technical aspects of the project. Secondly, concerted attempts are being made to involve the public at all stages of the project. It will therefore be essential for the principal investigator and assistants to be sensitive to the complexities of this situation. Furthermore, it is desirable that everyone in the area participate in the study in order to arrive at valid conclusions. Submitted proposals should detail how these concerns will be dealt with in a cost-effective manner.

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III. Project Objectives

The following are the main objectives for the project:

1. To determine the nature and magnitude of health problems in the study area, including cancer and mortality rates.
2. To identify geographic clustering of health effects if they exist.
3. To determine which health effects may be causally related to exposure to environmental contaminants.
4. To determine possible causes for health effects of interest in #3.
5. To identify individuals requiring clinical evaluation and ensure their treatment through an appropriate referral system.
6. To review existing biophysical data relevant to the area for its usefulness in assessing the impact of acid-forming emissions and associated compounds on human health.

IV. Study Area Facts

1. Communities involved: Hillspring, Glenwood, Mountainview, Twin Butte and surrounding areas (see attached map).
2. Surface area: 550 square miles.
3. Location: approximately 140 miles southwest of Calgary, Alberta (2-1/2 hours driving time).
4. Current population size of study area: 2228 (about 620 families).
5. Minimum number of outmigrants (approximate): 1827.
6. Elevation: 3800 feet at Pincher Creek.
7. Sour gas processing plants:
    a. operating: Shell-Waterton Gas Plant
    b. no longer operating: Gulf-Pincher Creek Gas Plant (as of 1983).

V. The Project

The project can be broken down into the following sub-projects:

1. epidemiological review of dire health consequences
2. clinical diagnostic review
3. environmental data review

Proponents are encouraged to respond to all or parts of the project according to their respective expertise, with recommendations for sub-contracting other parts if necessary. It should be noted, however, that sub-projects (1) and (2) contain intrinsic linkages which should not be separated without documentation.

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NOTE: The principal investigator will be provided with the retrospective cohort including names and locations of all out-migrants located by that time. Due to the anticipated difficulty of tracing and contacting out-migrants, proponents should outline in some detail how this task will be accomplished successfully using methods that are acceptable to the public and the SAB.

The sub-projects are detailed as follows:

1. Epidemiological review of dire health consequences

The SAB identified three main dire health concerns of residents in the study area following meetings with the public and a review of reports available to them. These were excess cancer, high mortality rates and adverse pregnancy outcomes.

To address these concerns at the community and individual level the SAB recommended a retrospective cohort study of mortality which must account for outmigration over the period 1959 to the present. Although the primary focus of this aspect of the project is the residents of the study area, the boundaries are not rigid and can include other residents. The retrospective cohort will be provided by the Project Manager who will also facilitate access to individual death certificates and other relevant databases (eg. church records).

To address the increased cancer incidence concern existing vital statistics and cancer incidence data should be used to identify the nature and magnitude of the cancer problem in the study area. This aspect of the project can be accomplished by using the retrospective cohort provided above and reviewing all cases appearing in the Alberta Cancer Registry and on lists provided voluntarily by residents in the study area.

To address concerns about pregnancy outcomes, outcomes should be evaluated by calculation of birth and fetal mortality rates and by an assessment of birth weights, birth defects, and the number of premature infants.

Development and interpretation of all data for the above analyses must take into account potentially confounding demographic factors (eg. religious type and distribution, smoking and nutritional habits, immigration/emigration patterns, etc.). Within area variability should also be examined along with the possible influence of genetic factors.

The anticipated outcome of this stage is a detailed report that will be subjected to SAB selected peer reviews and revisions.

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2. Clinical Diagnostic Review

The second subproject is the clinical diagnostic review. The SAB recommended a multi-stage approach to this subproject.

Stage 1: Using the retrospective cohort developed for the epidemiological studies, the first stage would involve the development of a comprehensive inventory of symptomatic health complaints of all residents currently living in the study area as well as a sufficient number of outmigrants necessary to define the nature and magnitude of the problem. The suggested mechanism for this step is an individual interview with each resident, using a standardized and validated clinical evaluation questionnaire supplemented with questions that will define more accurately other factors in the individual's microenvironment (eg. nutrition/water source(s), animal health, proximity to gas plants, etc.).

It is essential that the person(s) performing this work be trained in the collection of such data and be sensitive to the publics' concerns. It is also imperative that medical confidentiality be maintained and yet the data coded in such a way so as to: 1) permit the identification of individuals requiring further clinical evaluation; 2) permit data pooling and subsequent analysis; and 3) permit banking of data and project documents in the central data repository for the project. The anticipated outcome of this stage would be:

1) complete medical histories of each resident in the study area
2) identification of the nature and magnitude of the health problems
3) identification of geographic clustering of symptoms
4) identification of correlations influenced by microenvironmental factors
5) identification in the aggregate of individuals to be medically examined or tested.

Stage 2: Following a review of the health information obtained in Stage 1, the principal investigator will determine which residents require clinical follow-up. This may take the form of on-site clinical evaluation by a medical doctor or team of health professionals. This stage will provide routine clinical tests that can be performed accurately in the field (e.g. blood workups, pulmonary function, etc.). The suggested mechanism is the use of a portable clinical laboratory. Quality assurance of all data generated is a prerequisite of this work. This stage should include an evaluation of outmigrants if warranted.

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NOTE: In order to practice medicine legally within Alberta, all medical doctors must be placed on the courtesy registry of the Alberta Medical Association. A letter of good standing from your own medical association plus a current curriculum vitae must accompany each proposal.

Stage 3: It is anticipated that some individuals may require clinical evaluation using special diagnostic techniques not available through the portable laboratory or local medical facilities (eg. comprehensive allergy screens, CATSCANS, heavy metals analysis, etc.). It is suggested that this be accomplished through referrals to appropriate medical experts at major Alberta hospitals (i.e. in Calgary or Edmonton) or experts at medical centers outside of Alberta. In all cases the principal investigators must ensure the quality assurance of all data including documentation of reasons for the selection of the specialist, laboratory and diagnostic technique used.

One issue worthy of special mention at this point is the perception by residents of health problems caused by heavy metals exposure. Hair tissue analyses have been performed to date on some of the study area residents through Dr. E. Snider (University of Alberta sociologist), through Shell Canada Resources Ltd. and more recently through Gulf. Current results are conflicting, scientifically unacceptable or unavailable. Therefore, the SAB recommends that state of the art assays for heavy metal exposure be used to resolve this health concern. More specifically it is recommended that hair samples be obtained from all residents with suspected heavy metals problems and, where found necessary, from certain individuals participating in the clinical evaluation studies. The method of obtaining and preparing hair samples is to be specified exactly. Analyses are to be done using a validated specific method, one element at a time, by a recognized expert laboratory. Documentation of quality control and raw data must be available upon request.

Elements of primary concern are lead (Pb), cadmium (Cd), mercury (Hg), and selenium (Se). In cases with abnormally high levels of lead, cadmium or mercury and/or low levels of selenium a follow-up should be performed and include analysis of: 1) red blood cells Pb levels; amino levulinic acid dehydratase activity; 2) urine and serum level of Cd or Hg; and 3) red blood cell and serum levels of Se as well as red blood cell glutathione peroxidase activity. These tests may be supplemented by other scientifically acceptable assays.

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If other metals are tested for (eg. nickel) and found to be abnormally high, similar attempts should be made to delineate body burden and significant biological effects.

Stage 4: Expected output; compilation of all data and preparation of a detailed report that will be subject to SAB selected peer review and revision.

NOTE: All respondents to the RFP must include details of how severe cases requiring immediate attention will be dealt with.

3. Environmental Data Review

Over the years some data has been collected in the study area with respect to levels of various compounds in soil, water, vegetation and the atmosphere. These data have not been reviewed from a medical/toxicological standpoint to date with regard to adequacy, the geographic distribution of potential pollutants, information gaps, etc. The objectives of this subproject are:

a. to establish the usefulness of existing biophysical data in assessing the impact of acid-forming emissions and associated compounds on human health in the study area.
b. to identify gaps in the data where further monitoring studies are warranted and specify approaches for obtaining the needed information.
c. to correlate, where possible, any existing patterns of potential pollutant distribution with health effects data collected in subprojects 1 to 3 previously mentioned.

Copies of all relevant documents and monitoring data are presently being brought together in one location. The review team should consist of at least one medical professional with toxicological expertise and an analytical chemist. Of specific interest to the overall project are levels of heavy metals, H_2S, SO_X, NO_X, O_3 and particulates although interviews with the public may reveal other substances as well. A list of available information is attached.

The expected output will be a detailed report subject to SAB selected peer review and revision.

NOTE: Subproject 3 may be subcontracted in consultation with the Project Manager.

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VI. Project Schedule

The following is the suggested time schedule for the Project:

Activity	Completion target date
1. SAB review of proposals	early February, 1985
2. Final selection of principal investigator and letting of contract	March, 1985
3. Completion of epidemiology studies and environmental data review	August 31, 1985
4. Completion of stages 1 and 2 of clinical diagnostic review	September 30, 1985
5. Completion of stage 3 of clinical diagnostic review	October 31, 1985
6. Submission of preliminary report	October 31, 1985
7. Submission of final report	To be arranged

VII. Project Budget

A detailed budget to be submitted with proposal.

VIII. Reporting Requirements

In addition to regularly scheduled verbal reports to the Project Manager, the following written reports will be required under the awarded contract:

1. Progress Reports (10 copies). Following commencement of the contract, a comprehensive quarterly report shall be submitted to the Project Manager reflecting all activity conducted during each reporting period, a summary of data in sufficient detail to be reviewed by the SAB, and a detailed statement of proportion of project objectives achieved and monies spent.

2. Preliminary Report (10 copies). A preliminary report to the Project Manager (by October 31,1985) shall present an outline of the preliminary conclusions and interpretation of the data collected.

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3. Final Report (10 copies). A final report to the Project Manager shall present, in depth, all activities conducted during the contract from initiation to conclusion as well as an in depth presentation and interpretation of all data collected. The report shall be written in a formal style that will permit its use as a reference document. Copies of the report shall be presented simultaneously to the Alberta Government and the Acid Deposition Research Program.

4. Statement of Expenditures (3 copies). Detailed statements of expenditures shall be submitted to the Project Manager every two (2) months.

IX. Submission of Proposals

Seven (7) copies of the proposal should be submitted to:

Robert E. Rogers, Ph.D.
Project Manager,
Medical Diagnostic Review Project
Acid Deposition Research Project
c/o Concordia College
7128 Ada Boulevard
Edmonton, Alberta
Canada
T5B 4E4

The deadline for receipt of proposals is January 31, 1985.

Appendix 5.1.5.3

DETAILED METHODS OF BIOCHEMICAL ANALYSIS

Foothills Hospital

1403 - 29 St. N.W.
CALGARY, ALBERTA T2N 2T9
(403) 270-1110

1985 10 07

Dr. Dales
Purvis Hall
McGill University
1020 - Pine Avenue West
Montreal, PQ
H3A 2B4

Dear Dr. Dales:

The methods used for the attached analysis is provided by Technicon Instruments Corporation and are done on the SMAC II instrument.

To Quality Control the instrument, data from SMAC is monitored using a normal and abnormal control product. These are sampled every 16 patient samples. Criteria to reject or accept values are based on the Westgaard Rule system. SMAC is recalibrated every 96 patient samples and the baseline is checked every 48 patient samples to ensure that no drifts occur.

As well, external Quality Control samples are measured on a regular basis to ensure consistency with other SMAC users and similar method protocols.

I hope this will provide you with the information you require. If you need any further assistance, please don't hesitate to contact me.

Yours sincerely,

Dan Lesick

D. Lesick, DHT
Chemical Pathology

DL:ldf

Enclosure

Albumin	Doumas, Watson and Biggs - BCG method
Alkaline phosphatase	Bessy, Lowry and Brock - PNPP
Aspartate transaminase	Henry, Chiamori, Berkman - NaDH
Calcium	Gatelman - 8 Hydroxyquinoline and cresolphtalein complexone
Carbon Dioxide	Skeggs and Hochstrasser
Chloride	Zall, Fisher and Garner - Mercuric Thiocyanate
Cholesterol	Allan, Poon, Chan, Richmond and Fu - Oxidase
Creatine phosphokinase	Siegel and Cohen ADP-CPK substrate
Creatinine	Jaffe - Picric Acid
Glucose	Hexokinase
Inorganic phosphate	Daly and Erlingshausen - phosphomolybdate complex
Lactic Dehydrogenase	Wacker, Ulmer and Vallee - NaD
Potassium	Rao - Pelavin and Morgenstern - ISE
Sodium	Rao - Pelavin and Morgenstern - ISE
Total Bilirubin	Jendrassik and Grof - Caffeine sodium benzoate
Total Protein	Skeggs and Hochstrasser - Biuret
Urea	Match et al - Diacetyl Monoxime
Urate	Leon, Smith, Snyder and Horvath - Uricase

Appendix 5.1.6

CLINICAL ALGORITHMS USED TO DEFINE THE SPECIFIC CONDITIONS LISTED IN TABLE 13.4.1.3/2

APPENDIX 5.1.6
CLINICAL ALGORITHMS USED TO DEFINE THE SPECIFIC CONDITIONS LISTED IN TABLE 13.4.1.3/2

General Approach Used to Construct Algorithms

1) Symptoms, signs, and/or physiological abnormalities used.

2) Combinations of variables and data sources used where possible.

3) "Cut point" chosen to reduce the false positive rate at expense of increasing the false negative rate. Exceptions where more than one "cut point" is used are indicated by "possible", "probable" and "definite" degrees of certainty of condition.

4) Validation - content (Drs. R. Dales, S. Gauthier, M. Schechter, W.O. Spitzer, N. Steinmetz, P. Tousignant)
   - criterion - certain algorithms are the clinical criterion (i.e. high measured blood pressure is arterial hypertension)

5) Reproducibility - limited by reliability of data sources

OCULAR

Conjunctivitis: "probable" = itching, burning or watering of the eyes in the last 2 weeks

"definite" = "probable" AND conjunctiva definitely red on examination bilaterally

CUTANEOUS

Dermatitis: "possible" = itching or burning of the skin in the last 2 weeks

"probable" = "possible" AND definite bilateral skin rash

"definite" = "probable" AND skin rash red in colour

NEUROLOGICAL

Peripheral Neuropathy:

"symptomatic" tingling or loss of feeling in hands, feet, fingers or toes every day during the past 2 weeks,

AND

ankle reflexes reduced or absent bilaterally,

AND

vibration sense reduced or absent in great toes bilaterally

"asymptomatic" no tingling or loss of feeling in hands, feet, fingers or toes every day during past 2 weeks,

AND

loss of ankle reflexes bilaterally,

AND

loss of vibration sense in great toes bilaterally.

Mononeuropathy

Sensory component: tingling or loss of feeling in hands, feet, fingers or toes every day in past 2 weeks,

AND

sensation to pin in feet or hands different between right and left side, or, reduced or absent on either side

Motor component: weakness in extremity,

AND

(deep tendon reflexes reduced or absent on one side only) OR (reduced muscle strength on one side only).

Tremor

Essential: daily trembling or unsteadiness of the hands,

AND

action tremor present on both right and left side,

AND

dysmetria not present,

AND

ataxia not present,

AND

muscle tone not flaccid or spastic

NOTE: Algorithms were constructed for cerebellar and parkinsonian tremor. Together they detected less than 1% of all participants and thus were deleted.

RESPIRATORY

Rhinitis: "probable" = itching, burning or running nose not due to a cold in the last 2 weeks

"definite" = "probable" AND definite nasal mucosal redness or edema

Pharyngitis: "probable" = irritation of the throat not due to cold

"definite" = "probable" AND definite redness or edema of the pharynx

Chronic bronchitis: sputum production on most days for ≥ 3 consecutive months for ≥ 2 years

Wheezing syndrome: "grade 1" = wheeze apart from colds OR wheezing on most days or nights

"grade 2 " = "possible" AND more than 1 episode of wheeze with dyspnea

"grade 3" = "probable" AND a diagnosis of asthma was confirmed by a doctor

Arterial Hypertension: positive response to "Do you presently have high blood pressure?" and positve response to "Yesterday or the day before did you take or use...medicine for the heart or blood pressure?"

OR

blood pressure measured at $\geq$ 105 mm Hg diastolic during study

Complicated Arterial Hypertension:
"arterial hypertension" present

AND

(definite electrocardiographic evidence of left ventricular hypertrophy in the absence of a cardiac murmur) OR (definite "copper or silver wiring" present in ocular fundi) OR (serum urea $\geq$ than 9.2 mmol/L)

OBESITY

$$\frac{\text{Weight (kg)}}{\text{Height (m)}^2} \quad >27 \text{ in males or } >25 \text{ in non-pregnant females}$$

DEAFNESS

Ticking stopwatch (normally heard 4 m away) not heard $\leq$ 2.5 cm from ear

BACK PAIN

Any back pain = present complaint of trouble with back or spine

With any neurological signs = "any back pain" AND [(deep tendon reflexes hypoactive or absent) OR (reduced muscle bulk in calf or thigh) OR (reduced or absent sensation to pin in feet or legs)]

HEART MURMUR

Systolic = systolic murmur definitely heard over heart
Diastolic = diastolic murmur definitely heard over heart with or without a systolic murmur

Appendix 8.1.1

DETAILED TRACE METAL LABORATORY METHODS

Appendix 8.1.1/1

DETAILED LABORATORY METHODS
CENTRE DE TOXICOLOGIE DU QUEBEC, QUEBEC, CANADA

Centre de Toxicologie du Québec

DOSAGE DE L'ARSENIC DANS LES CHEVEUX

DOMAINE D'APPLICATION

Cette méthode permet de doser l'arsenic dans les cheveux, ceux-ci étant dissous dans une solution d'acide nitrique concentré.

PRINCIPE

L'arsenic est dosé par absorption atomique (four au graphite).

MATERIEL

- Spectrophotomètre à absorption atomique Perkin-Elmer, modèle 5000, avec un correcteur de bruit de fond au deutérium.
- Four au graphite Perkin-Elmer, modèle 500 avec échantillonneur automatique AS-40.
- Lampe EDL d'arsenic Perkin-Elmer
- Micropipettes Eppendorf de 10, 100, 200 et 500 µl

MATERIEL (suite)

- Pipettes jetables de 1 et 10 ml.
- Tube Falcon de BD #2070
- Godets jetables de 500 µl ou 1 ml en polystyrène Fisher #2-544-2 ou #2-544-19.
- Tube au graphite non recouvert de carbone pyrolitique (non-pyrolitique).

REACTIFS

- Acide nitrique concentré Baker #5-9603 "Suitable for mercury determination".
- Eau distillée déminéralisée.
- Acide nitrique 0.5%:
  - Ajouter 5 ml de HNO_3 à 1 litre d'eau distillée déminéralisée.
- Solution mère d'arsenic 1000 µg/ml (1000 ppm) Fisher SO-A-449
- Solution: 10 µg/ml (10 ppm):
  - Ajouter 1 ml d'une solution mère d'arsenic 1000 ppm dans un ballon jaugé de 100 ml.
  - Compléter avec de l'acide nitrique 0.5% jusqu'au trait de jauge.
  - Bien mélanger.

REACTIFS (suite)

- Solution: .1 µg/ml (.1 ppm)

  - . Ajouter 1 ml d'une solution de 10 ppm dans un ballon jaugé de 100 ml.
  - . Compléter avec de l'acide nitrique 0.5% jusqu'au trait de jauge.

- Nitrate de nickel ($Ni(NO_3)_2$)

  - . Ajouter 5 g de nitrate de nickel dans 500 ml d'eau distillée déminéralisée.

Etant donné que la concentration en arsenic dans les cheveux est inférieure à 1 µg/g en moyenne, on prépare une solution étalon dont la concentration en plomb est équivalente à 10 mg de cheveux contenant 1 µg/g d'arsenic dans une solution finale.

Si la lecture de l'échantillon est élevée plus de 1% que la lecture du standard, il faut faire l'une des deux choses suivantes:

1) soit recalibrer avec un standard ayant une plus forte concentration;
2) soit diluer notre échantillon avec du $Ni(NO_3)_2$ à partir de la solution mère (digérat de cheveux).

Standard:

Ajouter dans un godet: 500 µl de HNO_3 concentré
100 µl de std As .1 µg/ml
400 µl de $Ni(NO_3)_2$

PROTOCOLE ANALYTIQUE

Ajustement des paramètres instrumentaux: Absorption atomique 5000

- Puissance de la lampe EDL : 8 Watts
- Longueur d'onde : 193.7 mm
- Fente Low : 0.7 mm
- Correcteur de bruit de fond : allumé
- Imprimante : allumée
- Temps de lecture : 2.0 secondes
- Mode : peak Ht Conc.
  AABG
- Expansion : 1
- Sl (standard #1) : 1.0
- Energie de la lampe : 54-58

Four au graphite 500

- Séchage : 35 sec. à 130°C
  + 12 sec. à 350°C
- Carbonisation : 20 sec. à 900°C
- Atomisation : 5 sec. à 2700°C

Step	Temp (°C)	Ramp	Hold time	Read	Baseline	Int. flow
1	130	5	30	-	-	-
2	350	10	2	-	-	-
3	900	1	9	-	-	-
4	900	1	9	-	6	0
5	2700	0	5	0	-	0
6	2700	1	4	-	-	-

.PROTOCOLE ANALYTIQUE

Injecteur automatique AS-40:

- Sample volume : 20 µl
- Alternate volume : -
- Instrument programme (arsenic #1) : 1
- HGA programme (arsenic #1) : 1
- # Standard : 1
- Recal A : 16
- Recal B : 31
- Recal C : -
- Last sample : 35
- Séquence : 1

PREPARATION DES ECHANTILLONS

(voir protocole de lavage et digestion des cheveux).

Aprês digestion de 10 mg ± 1 mg de cheveux dans 500 µl d'acide nitrique concentré, diluer le digérat avec une quantité égale de $Ni(NO_3)_2$.

Exemple: 100 µl de digérat de cheveux
+ 100 µl de $Ni(NO_3)_2$

ou 500 µl de digérat de cheveux
+ 500 µl de $Ni(NO_3)_2$

VERIFICATION DES REACTIFS

Faire le programme à vide sur l'appareil et appuyer sur la touche "AZ".

Ensuite passer les solutions pour voir s'il y a contamination.

- Eau distillée déminéralisée
- Acide nitrique 0.5%
- Acide nitrique concentré
- $Ni(NO_3)_2$

CALIBRAGE

- Si le niveau de contamination est acceptable, mettre en position "AZ" sur l'échantillonneur le blanc contenant 500 µl d'acide nitrique concentré et 500 µl de $Ni(NO_3)_2$. Sinon refaire les solutions avec des réactifs plus propres.

- L'appareil fait son auto-zéro (zéro automatique) sur cette solution.

- Puis passer le standard qui doit donner une absorbance de l'ordre de 0.075±0.01 selon l'état du tube.

  * Consulter les résultats obtenus précédemment.

- Pour vérifier si notre standard et notre calibrage sont bons, passer une solution "stock" de cheveux digérés "basse" et une autre appelée "moyenne et/ou élevée". Cette dernière devra avoir un ajout d'une quantité connue d'arsenic et devra donner cette concentration. Sinon, vérifier les paramètres de l'appareil, le tube, l'arrivée des gaz, la lampe, refaire le standard, etc.

CALIBRAGE (suite)

Exemple de résultat:

		Abs
Blanc	=	.000
Standard	=	.079
Bas	=	.009
Moyen	=	.081

$$\frac{\text{Valeur du "moyen" - Valeur du "bas"}}{\text{Valeur du standard}} \times 100 = \% \text{ de recouvrement}$$

Si le standard est bien fait, on doit retrouver 90 ± 3% d'arsenic recouvré (avec de bonnes conditions sur l'appareil).

- Ensuite passer un digérat de cheveux et vérifier le $\boxed{\text{BG}}$. Celui-ci doit être entre 0.000 et 0.100. Si au début d'une série le $\boxed{\text{BG}}$ est déjà aux environs de 0.100, il faut vérifier fréquemment le $\boxed{\text{BG}}$ car à ce moment-là, c'est peut-être le tube qui est détérioré.

- Si le blanc est acceptable (absorbance <0.010), le standard donne une bonne absorbance (recouvrement de 90 ± 3%) et que le $\boxed{\text{BG}}$ du digérat de cheveux n'est pas trop élevé (0.000 à 0.100), on peut passer à l'étape suivante.

  * La courbe est linéaire jusqu'à une absorbance ≙ 0.370

LECTURE DES ECHANTILLONS

- Placer le blanc sur le plateau de l'échantillonneur à la position: AZ (auto-zéro)
  ou #0
  ou #40

LECTURE DES ECHANTILLONS (suite)

- Ensuite le standard à la position: S1
  ou #41

- Les témoins: Bas à la position: 1
  Moyen à la position: 2 - 16 - 31

- Les échantillons de la position 1 à 35

N.B. - Lorsqu'il y a un témoin élevé, placer à la position: 3

- Faire revenir l'échantillonneur à la position: AZ (auto-zéro) en enfonçant la touche "Reset".

- Puis appuyer sur le bouton "start" du AS-40. Celui-ci fait:
  - AZ (auto-zéro)
  - S1 (standard)
  - 1 - 15 (échantillons + témoins)
  - entre 15-16, il refait son calibrage (déjà programmé sur le AS-40 ("Recal A")).
  - 16-30 (échantillon + témoin)
  - entre 30-31, il refait son calibrage (déjà programmé sur le AS-40 ("Recal B")).

- Pour la roulette suivante, vérifier le $\boxed{\text{BG}}$ d'un digérat de cheveux et reprendre au début de la lecture des échantillons.

N.B. - Vérification du $\boxed{\text{BG}}$ = obligation de recalibrer.

CALCULS

Concentration d'arsenic/ cheveux en µg/g:

$$\frac{\text{Conc. lue} \times 10\ (\text{mg})}{\text{Poids de cheveux (mg)}}$$

LIMITE DE DETECTION

0.1 ppm/cheveux pour un échantillon de 10 mg.

OBSERVATIONS DIVERSES

Reproductibilité:

Lors de lecture de plusieurs standards ayant la même concentration et passé à 10 reprises chacun, si nous obtenons un coefficient de variation de 10% plus grand, vérifier les solutions et les paramètres.

PROBLEMES RENCONTRES

Ligne de base:

Vérifier constamment la ligne de base où peut apparaître des pics négatifs dus à une faiblesse de courant à certains moments donnés.

REFERENCES

- Savoie, Jean-Yves, Weber, Jean-Philippe, "Etudes de la distribution de certains toxiques dans la population de Rouyn-Noranda", Rapport pour les Services de Protection de l'Environnement, Février 1979.
- Perkin-Elmer, AS-40, Auto sampler sequence version, Mai 1979 (Operator's manual).
- Perkin-Elmer, Modèle 5000, Atomic Absorption Spectrophotometers, Mai 1978, (Operator's manual).
- Perkin-Elmer, HGA 500, Graphite Furnace, Juin 1978, Operator's manual.
- Perkin-Elmer, Analytical Methods using the HGA graphite furnace, Mars 1977.

Janvier 1980, Laboratoire de toxicologie, C.T.Q.

Centre de Toxicologie du Québec

DOSAGE DU CADMIUM DANS LES CHEVEUX

DOMAINE D'APPLICATION

Cette méthode permet de doser le cadmium dans les cheveux, ceux-ci étant dissous dans une solution d'acide nitrique concentré.

PRINCIPE

Le cadmium est dosé par absorption atomique (four au graphite).

MATERIEL

- Spectrophotomètre à absorption atomique Perkin-Elmer, modèle 5000, avec un correcteur de bruit de fond au deutérium.
- Four au graphite Perkin-Elmer, modèle 500 avec échantillonneur automatique AS-40.
- Lampe EDL de cadmium Perkin-Elmer.
- Micropipettes Eppendorf de 10, 100 , 200 et 500 µl

Le Centre Hospitalier de l'Université Laval - 2705, boul. Laurier, Québec, Qué. G1V 4G2
TÉL.: (418) 656-8326 (418) 656-8092 (laboratoire)

MATERIEL (suite)

- Pipettes jetables de 1 et 10 ml.

- Tube Falcon de BD #2070

- Godets jetables de 500 µl ou 1 ml en polystyrène Fisher #2-544-2 ou #2-544-19.

- Tube au graphite recouvert de carbone pyrolitique.

REACTIFS

- Acide nitrique concentré Baker #5-9603 "Suitable for mercury determination".

- Eau distillée déminéralisée.

- Acide nitrique 0.5%:
    - . Ajouter 5 ml de HNO_3 à 1 litre d'eau distillée déminéralisée.

- Solution mère de cadmium 1000 µg/ml (1000 ppm) Fisher SO-C-118.

- Solution: 10 µg/ml (10 ppm):
    - . Ajouter 1 ml d'une solution mère de cadmium 1000 ppm dans un ballon jaugé de 100 ml.
    - . Compléter avec de l'acide nitrique 0.5% jusqu'au trait de jauge.
    - . Bien mélanger.

REACTIFS (suite)

- Solution: .1 µg/ml (.1 ppm):

    - Ajouter 1 ml d'une solution de 10 ppm dans un ballon jaugé de 100 ml.
    - Compléter avec de l'acide nitrique 0.5% jusqu'au trait de jauge.

- Nitrate d'ammonium (4%):

    - Ajouter 2 g de nitrate d'ammonium dans 50 ml d'eau distillée déminéralisée.

Etant donné que la concentration en cadmium dans les cheveux est inférieure à 1 µg/g en moyenne, on prépare une solution étalon dont la concentration en cadmium est équivalente à 10 mg de cheveux contenant 1 µg/g de cadmium dans une solution finale.

Si la lecture de l'échantillon est élevée plus de 1% que la lecture du standard, il faut faire l'une des deux choses suivantes:

1) soit recalibrer avec un standard ayant une plus forte concentration;
2) soit diluer notre échantillon avec du NH_4NO_3 4% à partir de la solution mère (digérat de cheveux)

Standard:

Ajouter dans un godet: 500 µl de HNO_3 concentré
100 µl de std Cd 1 µg/ml
400 µl de NH_4NO_3 4%

PROTOCOLE ANALYTIQUE

Ajustement des paramètres instrumentaux: Absorption atomique 5000

- Puissance de la lampe EDL : 5 Watts
- Longueur d'onde : 228.6 mm
- Fente Low : 0.7 mm
- Correcteur de bruit de fond : allumé
- Imprimante : allumée
- Temps de lecture : 2.0 secondes
- Mode : peak Ht Conc. AABG
- Expansion : 1
- S1 (standard #1) : 1.0
- Energie de la lampe : 54 - 58

Four au graphite 500

- Séchage : 35 sec. à 130°C
  + 12 sec. à 350°C
- Carbonisation : 20 sec. à 600°C
- Atomisation : 5 sec. à 2000°C

Step	Temp (°C)	Ramp	Hold time	Read	Baseline	Int. flow
1	130	5	30	-	-	-
2	350	10	2	-	-	-
3	600	1	9	-	-	-
4	600	1	9	-	6	50
5	2000	0	5	0	-	50
6	2700	1	4	-	-	-

PROTOCOLE ANALYTIQUE

Injecteur automatique AS-40:

- Sample volume : 20 µl
- Alternate volume : -
- Instrument programme (cadmium #2) : 2
- HGA programme (cadmium #2) : 2
- # Standard : 1
- Recal A : 16
- Recal B : 31
- Recal C : -
- Last sample : 35
- Séquence : 1

PREPARATION DES ECHANTILLONS

(voir protocole de lavage et digestion des cheveux).

Après digestion de 10 mg ± 1 mg de cheveux dans 500 µl d'acide nitrique concentré, diluer le digérat avec une quantité égale de NH_4NO_3 4%.

Exemple: 100 µl de digérat de cheveux
+ 100 µl de NH_4NO_3 4%

ou 500 µl de digérat de cheveux
+ 500 µl de NH_4NO_3 4%

VERIFICATION DES REACTIFS

Faire le programme à vide sur l'appareil et appuyer sur la touche "AZ".

Ensuite passer les solutions pour voir s'il y a contamination.

- Eau distillée déminéralisée
- Acide nitrique 0.5%
- Acide nitrique concentré
- NH_4NO_3 (4%)

CALIBRAGE

- Si le niveau de contamination est acceptable, mettre en position "AZ" sur l'échantillonneur le blanc contenant 500 µl d'acide nitrique concentré et 500 µl de NH_4NO_3 4%. Sinon refaire les solutions avec des réactifs plus propres.

- L'appareil fait son auto-zéro (zéro automatique) sur cette solution.

- Puis passer le standard qui doit donner une absorbance de l'ordre de 0.25 ± 0.1 selon l'état du tube.

  * Consulter les résultats obtenus précédemment.

- Pour vérifier si notre standard et notre calibrage sont bons, passer une solution "stock" de cheveux digérés "basse" et une autre appelée "moyenne et/ou élevée". Cette dernière devra avoir un ajout d'une quantité connue de cadmium et devra donner cette concentration. Sinon, vérifier les paramètres de l'appareil, le tube, l'arrivée des gaz, la lampe, refaire le standard, etc.

CALIBRAGE (suite)

Exemple de résultat:

Abs

Blanc = .000
Standard = .263
Bas = .027
Moyen = .278

$$\frac{\text{Valeur du "moyen" - Valeur du "bas"}}{\text{Valeur du standard}} \times 100 = \text{\% de recouvrement}$$

Si le standard est bien fait, on doit retrouver 95 ± 3% de cadmium recouvré (avec de bonnes conditions sur l'appareil).

- Ensuite passer un digérat de cheveux et vérifier le $\boxed{BG}$. Celui-ci doit être entre 0.000 et 0.100. Si au début d'une série le $\boxed{BG}$ est déjà aux environs de 0.100, il faut vérifier fréquemment le $\boxed{BG}$ car à ce moment-là, c'est peut-être le tube qui est détérioré.

- Si le blanc est acceptable (absorbance <0.010), le standard donne une bonne absorbance (recouvrement de 95 ± 3%) et que le $\boxed{BG}$ du digérat de cheveux n'est pas trop élevé (0.000 à 0.100), on peut passer à l'étape suivante.

  * La courbe est linéaire jusqu'à une absorbance ± 0.600.

LECTURE DES ECHANTILLONS

- Placer le blanc sur le plateau de l'échantillonneur à la position: AZ (auto-zéro)
  ou #0
  ou #40

LECTURE DES ECHANTILLONS (suite)

- Ensuite le standard à la position: S1
  ou #41

- Les témoins: Bas à la position: 1
  Moyen à la position: 2 - 16 - 31

- Les échantillons de la position 1 à 35

N.B. - Lorsqu'il y a un témoin élevé, placer à la position: 3

- Faire revenir l'échantillonneur à la position: AZ (auto-zéro) en enfonçant la touche "Reset".

- Puis appuyer sur le bouton "start" du AS-40. Celui-ci fait:

  - . AZ (auto-zéro)
  - . S1 (standard)
  - . 1 - 15 (échantillons + témoins)
  - . entre 15-16, il refait son calibrage (déjà programmé sur le AS-40 ("Recal A")).
  - . 16-30 (échantillon + témoin)
  - . entre 30-31, il refait son calibrage (déjà programmé sur le AS-40 ("Recal B")).

- Pour la roulette suivante, vérifier le $\boxed{\text{BG}}$ d'un digérat de cheveux et reprendre au début de la lecture des échantillons.

N.B. - Vérification du $\boxed{\text{BG}}$ = obligation de recalibrer.

CALCULS

Concentration de cadmium/cheveux en µg/g:

$$\frac{\text{Conc. lue x 10 (mg)}}{\text{Poids de cheveux (mg)}}$$

LIMITE DE DETECTION

≙0.03 ppm/cheveux pour un échantillon de 10 mg.

OBSERVATIONS DIVERSES

Reproductibilité:

Lors de lecture de plusieurs standards ayant la même concentration et passés à 10 reprises chacun, si nous obtenons un coefficient de variation de 3% plus grand, vérifier les solutions et les paramètres.

Recouvrement:

Vu le bon recouvrement obtenu dans le cas du plomb (voir protocole sur le plomb) avec le NH_4NO_3, on peut supposer la même efficacité pour le cadmium.

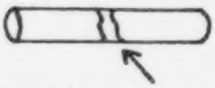
Temps de recouvrement à 600°C

Sans NH_4NO_3 = 10 sec. 66%
Avec NH_4NO_3 = 10 sec. 95%

PROBLEMES RENCONTRES

Tube:

- Non reproductibilité.
- Certains tubes qui après 25-50 échantillons se détérioraient rapidement (voir figure):



détérioration du tube au centre donne des variations lors de la lecture du standard.

PROBLEMES RENCONTRES (suite)

Ligne de base:

Vérifier constamment la ligne de base où peut apparaître des pics négatifs dus à une faiblesse de courant à certains moments donnés.

REFERENCES

- Savoie, Jean-Yves, Weber, Jean-Philippe, "Etudes de la distribution de certains toxiques dans la population de Rouyn-Noranda", Rapport pour les Services de Protection de l'Environnement, Février 1979.

- Perkin-Elmer, AS-40, Auto sampler sequence version, Mai 1979 (Operator's manual).

- Perkin-Elmer, Modèle 5000, Atomic Absorption Spectrophotometers, Mai 1978 (Operator's manual).

- Perkin Elmer, HGA 500, Graphite Furnace, Juin 1978, (Operator's manual).

- Perkin-Elmer, Analytical methods using the HGA graphite furnace, Mars 1977.

Centre de Toxicologie du Québec

Mercure total dans les cheveux

M-111 B

1. Domaine d'application.

Le taux de mercure dans un segment de cheveux est proportionnel au taux sanguin existant au moment de la formation de ce segment. On peut donc établir un profil de l'imprégnation mercurielle en fonction du temps par l'analyse de segments successifs d'une mèche de cheveux.

2. Principe et théorie.

Les segments de cheveux sont dissous dans une solution acide.

Le mercure est libéré de l'échantillon biologique par réduction et dosé ensuite par un détecteur U.V. (Le mercure contenu dans l'échantillon est transformé en un complexe soluble dans l'eau à l'aide de la L-cystéine). Le chlorure stanneux réduit le mercure à l'état métallique. Le chlorure de cadmium agit comme catalyseur pour briser le lien mercure-carbone (Hg-C) dans le cas du mercure organique. La méthode permet de doser le mercure total.

Les vapeurs sont entraînées par un courant d'air jusqu'à une cellule fermée placée dans le faisceau d'une lampe à mercure. La concentration est proportionnelle à l'absorbance lue.

3. Valeurs normales.

Population non-exposée: < 1 µg/g.

Linéarité. La méthode est linéaire jusqu'à 40 µg/g.

4. Limite de détection. Environ 0.2 µg/g.

5. Prélèvement.

Couper une mèche de cheveux ayant un diamètre de 5 mm à la racine du cuir chevelu. Fixer la mèche sur un carton à l'aide de broches en identifiant la racine et le bout. Déposer ensuite dans une enveloppe.

6. Matériel.

A) Matériel pour le montage du système:
- Pompe à circulation
- Tube tygon (5/16"O.D. 3/16 I.D.)
- Tube à essai à joint rodé 24/40 modifié par un embranchement à bouchon vissant pour l'introduction de l'échantillon
- Tube à dessicateur (pour l'anhydrone)
- Vortex-Genie (agitateur)
- Chronomètre (Gralab 600)
- Support universel
- Débimètre
- Ruban chauffant avec rhéostat
- Appareil U.V. Pharmacia Mercury Monitor, Model 100
- Multiprise
- Enregistreur Perkin-Elmer

B)
- Fioles jaugées 100 mL
- Pipettes sérologiques jetables de 1 mL et 2 mL
- Pipettes Eppendorf 10 µL, 20 µL, 100 µL, 500 µL
- Laine de verre
- Four micro-ondes Hotpoint
- Tubes en verre "Maple leaf" 12 x 75
- Gabarit

7. Solutions étalons.

- Solution étalon 1000 µg/mL (Fisher SO-M-114)
- Solution étalon: 0.2 µg/mL:
  Prélever 20 µL de mercure 1000 µg/mL. Transférer dans une fiole jaugée de 100 mL et compléter à la marque avec de l'eau distillée et déminéralisée.

8. Courbe d'étalonnage.

Préparer une courbe d'étalonnage en dosant successivement 0, 10, 20 µL d'une solution étalon de 0.2 µg/mL de mercure.On considère, aux fins de calculs, qu'il s'agit d'un 20 et d'un 40 (nanogrammes).

9. Réactifs.

Note: Les réactifs sont changés à chaque mois.

- Solution L-cystéine 1%, Baker 5-G122.
  Dissoudre 1 g de L-Cystéine, compléter à 100 mL avec de l'eau distillée et déminéralisée.

- Hydroxyde de sodium 45% (NaOH), Baker 1-3726.
  Dans un bécher de 2 litres contenant 750 mL d'eau déionisée, dissoudre un pot de NaOH (453 g). Laisser refroidir, puis compléter à 1 litre.

  N.B.: Réaction exothermique: placer le bécher dans un bain de glace sous la hotte.

- Solution chlorure de sodium 1% (NaCl), Baker 1-3624.
  Dissoudre 10 g de NaCl, compléter à 1 litre avec de l'eau distillée et déminéralisée.

- Solution de chlorure stanneux et chlorure de cadmium: $SnCl_2$ (Fisher T-142), $CdCl_2$ (Baker 1-1208).
  Dissoudre en chauffant très légèrement 50 g de $SnCl_2$ dans 20

- Anhydrone.
  Perchlorate de magnésium Mg $(ClO_4)_2$, Baker 1-0828.
  Passer au tamis afin de réduire les grains.

  N.B.: Ne pas utiliser chlorure de calcium ($CaCl_2$) ou Drierite. Il faut renouveler le tube dessicateur à chaque jour.

- Octanol.
  Octyl alcohol, Baker 1-9085.

- Acide nitrique concentré. Baker 9598-3 "Instranalyzed".

10. Conditions instrumentales.

- Appareil: U.V. Pharmacia Mercury Monitor, Model 100 avec photodétecteur.

- Description de l'appareil.

  Le réacteur est fait d'un tube à essai à joint rodé 24/40, modifié par l'addition d'un bras latéral pour permettre l'introduction de l'échantillon. Le réacteur est placé sur un agitateur "Vortex-Genie" commandé par une minuterie. Un robinet à quatre voies permet de diriger l'air provenant de la pompe vers le détecteur soit en court-circuitant le réacteur ou à travers le réacteur (position "analyse"). Un tube à dessicateur placé entre le réacteur et le détecteur sert à capter la vapeur d'eau. Le signal généré par le détecteur lors du passage du mercure est inscrit sur l'enregistreur.

- Paramètres.

Longueur d'onde:	254 nm
Power:	ON
Sensibilité:	0.04 mV
Zéro:	0-20
Polarité:	Négative
Enregistreur:	Sensibilité: 10 mV Vitesse du papier: 5

11. Préparation de l'échantillon.

- Séparation en segments de longueur voulue.

  Placer la mèche de cheveux sur le gabarit. Couper des segments de 1 cm.
  Peser à 0.1 mg environ 10 mg de cheveux dans un tube en verre, "Maple Leaf Brand" 12 x 75.

- Digestion à l'acide nitrique.

  - À l'aide d'une repipette ajouter 500 µL de HNO_3 concentré.

    Pour chaque série de digestions ajouter un blanc réactif contenant seulement HNO_3.

    Fermer les tubes et les placer sur un portoir.

    La digestion peut se faire sur une période de 24 heures ou plus rapidement. Sur une période de 24 heures, il s'agit de laisser reposer les tubes durant la nuit jusqu'à digestion presque totale du segment de cheveux. On finalise la digestion en faisant chauffer très légèrement (par période de 30 secondes environ) à basse température au four micro-ondes. Le digérat doit être clair. La digestion peut être effectuée plus rapidement en utilisant le four micro-onde dès le départ. De nouveau, il faut chauffer par courtes périodes seulement. En procédant lentement, et en surveillant attentivement, la technique requiert environ 30 minutes.

  - Faire refroidir à la température de la pièce ou dans un bain de glace.

  - Ajouter 500 µL d'H_2O, bien agiter.

12. Dosage.

- Dans un tube à joint rodé 24/40 ajouter successivement:
  - 1 mL de L-cystéine 1%
  - 5 mL de NaCl 1%
  - 10 mL de NaOH 45%
  - 500 µL de $SnCl_2$-$CdCl_2$
  - 3-4 gouttes d'Octanol

- Placer sous l'aérateur.

- Laisser agiter 1 minute au Vortex.

- Ouvrir le robinet. Lorsque la plume de l'enregistreur est revenue à la ligne de base, fermer le robinet.

- Ajouter 100 µL de l'échantillon (digérat acide).

- Laisser agiter 1 minute au Vortex.

- Ouvrir le robinet. Faire barboter jusqu'à ce que la ligne de base reprenne sa position initiale.

Préparer une courbe en dosant successivement 0, 10, 20 µL d'une solution étalon de 0.2 µg/mL de mercure. (Donc: 0,20 et 40 nanogrammes).

N.B.: Il est nécessaire d'éliminer le mercure contenu dans les réactifs avant d'analyser les inconnus (en faisant agiter les réactifs seuls et en laissant barboter jusqu'au retour à la ligne de base). Cette opération doit être répétée lorsqu'un inconnu a un taux élevé de mercure.

Une série de réactifs peut servir pour environ 15 échantillons selon de la qualité des réactifs ou la valeur des résultats obtenus. Lorsque l'enregistreur ne donne plus de signal, on doit changer les réactifs.

On doit passer un point de courbe à tous les 7 échantillons ainsi que lors du changement de réactifs afin de vérifier la stabilité du système.

13. Calculs.

- Déterminer la pente de la courbe d'étalonnage par moindres carrés sur ordinateur ou par une méthode graphique.

- Calculer la concentration de mercure dans les cheveux (µg/g) en appliquant la formule suivante:

$$\text{Concentration de Hg/cheveux } (\mu g/g) = \frac{\text{Hauteur du signal (mm)}}{\text{Pente x poids cheveux (mg)}}$$

14. Contrôle de qualité

Il existe 2 contrôles disponibles en tout temps. Voir le cahier des contrôles pour les détails. Lorsque la teneur obtenue dépasse de ± 10% la teneur réelle des contrôles il faut rejetter les résultats.

15. Description du gabarit utilisé pour couper les cheveux.

Le gabarit est formé d'une base en aluminium de 40 x 10 cm. Une bande de plastique dur de 40 x 4 cm est collée sur la partie avant de la base. Des clés rectangulaires de 9.5 mm de largeur, espacées de .5 mm pivotant à une extrémité viennent s'appuyer sur la base. La mèche de cheveux est placée sur la bande de plastique et les clés sont rabattues par dessus, tenant ainsi les cheveux fermement en place. La première clé est relevée et les cheveux sont coupés avec un scalpel au ras de la clé voisine. Les cheveux coupés sont placés dans un contenant étiquetté.

Détail du calcul

L'étalonnage est construit en injectant 0,10 et 20 µL de l'étalon 200 µg/L. Ceci correspond donc à 0,2 et 4 nanogrammes

Pour simplifier les calculs subséquents, on considère qu'il s'agit de 0,20 et 40 nanogrammes.

Ce sont ces valeurs qui sont utilisées pour calculer la pente, $m_{apparente}$

Il faut tenir compte du fait que

$$m_{reelle} = 10 \times m_{apparente}$$

Le poids de mercure contenu dans le digérat (1 ml) est obtenu (pour une injection de 100 µL) par:

$$Hg_{digerat}\ (ng) = 10 \times \frac{(H\ \text{échantillon})}{10\ m} = \frac{H}{m}$$

où H est la hauteur du signal de l'échantillon (mm) et m est la pente (apparente).

La concentration finale (µg/g ou ng/mg)
de l'inconnu devient alors:

$$c\ Hg_{inconnu}\ (\mu g/g) = \frac{H}{m_{approuvé}\ .\ \text{poids cheveux (mg)}}$$

17. Références.

EBBESTADT V., GUNDERSON and TORGRIMSEN T.A.
Simple method for the determination of inorganic mercury and methylmercury in biological samples by flameless atomic absorption.
Atomic absorption newsletter 14(6), Nov-Dec 1977, 142-143.

Révisé: Octobre 1983, par Sylvie Rodrigue, puis mai 1985, par Michel Lefebvre. La version B détaille l'étalonnage et les calculs.

Relu et approuvé par: Michel Lefebvre: Michel Lefebvre

Ghislaine Harvey: Ghislaine Harvey.

J.-Philippe Weber: ____________

Centre de Toxicologie du Québec

Mercure sanguin (total et organique)

Domaine d'application.

Le dosage du mercure sanguin sert à évaluer la quantité de mercure contenu dans l'organisme. Le taux sanguin est une mesure de l'imprégnation mercurielle au moment du prélèvement et reflète l'exposition à court terme, la demi-vie du méthyl-mercure dans le sang étant d'environ 70 jours.

Le domaine d'application optimal se situe entre 2 µg/L et 40 µg/L.

Principe et théorie.

Le mercure est libéré de l'échantillon biologique par réduction et dosé ensuite par un détecteur U.V.

Dans l'échantillon biologique le mercure se trouve lié à un groupement thiol (S-H). Le chlorure stanneux ($SnCl_2$) brise le lien mercure-soufre (Hg-S) et réduit ensuite le mercure à l'état métallique. Dans le cas du mercure organique il faut également briser le lien mercure-carbone (Hg-C) ce qui requiert l'addition de chlorure de cadmium ($CdCl_2$) comme catalyseur. La méthode permet donc de mesurer le mercure inorganique (avec $SnCl_2$ comme réducteur) ou le mercure total (mélange $SnCl_2$-$CdCl_2$ comme réducteur). Par différence on peut alors déduire la quantité de mercure organique contenu dans l'échantillon.

Les vapeurs sont entraînées par un courant d'air jusqu'à une cellule fermée placée dans le faisceau d'une lampe à mercure. La concentration est proportionnelle à l'absorbance lue.

Valeurs normales.

Population non-exposée: < 20 µg/L.

Linéarité.

La méthode est linéaire jusqu'à 40 µg/L.

Limite de détection. Environ 2 µg/L.

Prélèvement.

Le dosage est effectué sur du sang entier. On doit utiliser pour le prélèvement des tubes héparinés (Monoject, bouchon vert) ou des tubes metal free (BD-6527-bouchon marine).

Les tubes EDTA (bouchon lavande) ne doivent pas être utilisés pour le prélèvement, ils contiennent des substances interférentes.

Matériel.

A) Matériel pour le montage du système Hg.
  - Pompe à circulation
  - Tube tygon (5/16"O.D. 3/16 I.D.)
  - Tube à essai à joint rodé 24/40 modifié par un embranchement à bouchon vissant pour l'introduction de l'échantillon
  - Tube à dessicateur (pour l'Anhydrone)
  - Vortex-Genie (agitateur)
  - Chronomètre (Gralab 600)
  - Support universel
  - Débimètre

- Ruban chauffant avec rhéostat
- Appareil U.V. Pharmacia Mercury Monitor, Model 100
- Multiprise
- Enregistreur Perkin-Elmer

B)
- Fioles jaugées 100 mL
- Tubes Falcon 50 mL
- Pipettes sérologiques jetables de 1 mL, 2 mL, 5 mL
- Pipettes Eppendorf 50 µL, 100 µL, 200 µL, 500 µL
- Pipette SMI 200 µL
- Laine de verre

Solutions étalons.

- Solution mère 1000 µg/mL (Fisher SO-M-114)
- Étalon de mercure: 0.5 µg/mL:
  Prélever 50 µL de la solution mère de 1000 µg/mL. Transférer dans une fiole jaugée de 100 mL et compléter à la marque avec de l'eau distillée et déminéralisée.

Courbe d'étalonnage.

Pour la courbe de mercure sanguin, utiliser un pool de sang hépariné.

Préparation de la courbe.

Conc. Hg µg/L	Volume de sang (pool)	Volume solution Hg 0.5 µg/mL
Blanc	5.00 mL	0
5 µg/L	4.95 mL	50 µL
10 µg/L	4.90 mL	100 µL
20 µg/L	4.80 mL	200 µL

Les points de courbe sont conservés à 4°C pour une période d'environ 1 mois. Ils sont analysés comme des échantillons.

Réactifs.

Note: Les réactifs sont changés à chaque mois.

- Solution L-cystéine 1%, Baker 5-G122.
  Dissoudre 1 g de L-cystéine, compléter à 100 mL avec de l'eau distillée et déminéralisée.

- Hydroxyde de sodium 45% (NaOH), Baker 1-3726.
  Dans un bécher de 2 litres contenant 750 mL d'eau déionisée, dissoudre un pot de NaOH (453 g). Laisser refroidir, puis compléter à 1 litre.

  N.B.: Réaction exothermique: placer le bécher dans un bain de glace sous la hotte.

- Solution chlorure de sodium 1% (NaCl), Baker 1-3624.
  Dissoudre 10 g de NaCl, compléter à 1 litre avec de l'eau distillée et déminéralisée.

- Solution chlorure stanneux et chlorure de cadmium: $SnCl_2$ (Fisher T-142), $CdCl_2$ (Baker 1-1208).
  Dissoudre en chaffant très légèrement 50 g de $SnCl_2$ dans 20 mL d'eau distillée et déminéralisée.
  Ajouter 10 g de $CdCl_2$.
  Compléter à 100 mL avec de l'eau distillée et déminéralisée après dissolution du $CdCl_2$.

- Anhydrone. Baker 1-0828.
  Perchlorate de magnesium $Mg(ClO_4)_2$.
  Passer au tamis afin de réduire les grains.

  N.B.: Ne pas utiliser chlorure de calcium ($CaCl_2$) ou Drierite. Il faut renouveler le tube dessicateur à chaque jour.

- Octanol. Baker 1-9085.
  Octyl Alcohol.

Conditions instrumentales.

- Appareil: U.V. Pharmacia Mercury Monitor, Model 100 avec photodétecteur.

- Description de l'appareil.

Le réacteur est fait d'un tube à essai à joint rodé 24/40, modifié par l'addition d'un bras latéral pour permettre l'introduction de l'échantillon. Le réacteur est placé sur un agitateur "Vortex-Genie" commandé par une minuterie. Un robinet à quatre voies permet de diriger l'air provenant de la pompe vers le détecteur soit en court-circuitant le réacteur ou à travers le réacteur (position "analyse"). Un tube à dessicateur placé entre le réacteur et le détecteur sert à capter la vapeur d'eau. Le signal généré par le détecteur lors du passage du mercure est inscrit sur l'enregistreur.

- Paramètres.

Longueur d'onde:	254 nm
Power:	ON
Sensibilité:	0.04 mV
Zéro:	0-20
Polarité:	Négative
Enregistreur:	Sensibilité: 10 mV
	Vitesse du papier: 5

Préparation de l'échantillon. (Mercure total)

- Dans un tube à joint rodé 24/40 ajouter successivement:
  - 1 mL de L-cystéine 1%
  - 5 mL de NaCl 1%
  - 10 mL de NaOH 45%
  - 500 µL de $SnCl_2$-$CdCl_2$
  - 3-4 gouttes d'octanol

- Placer sous l'aérateur (robinet à quatre voies).

- Laisser agiter 2 minutes au Vortex.

- Ouvrir le robinet. Lorsque la plume de l'enregistreur est revenue à la ligne de base, fermer le robinet.

- À l'aide d'une pipette SMI ajouter 200 µL de l'échantillon. Rincer la pipette dans la solution.

- Laisser agiter 2 minutes au Vortex.

- Ouvrir le robinet. Faire barboter jusqu'à ce que la ligne de base reprenne sa position initiale.
  N.B.: Les points de courbe sont traités de la même façon qu'un inconnu. La pipette SMI est rincée entre chaque échantillon dans du NaCl 1%.

Il est nécessaire d'éliminer le mercure contenu dans les réactifs avant d'analyser les inconnus (faire agiter les réactifs seuls et laisser barboter jusqu'au retour à la ligne de base). Cette opération doit être répétée lorsqu'un inconnu a un taux élevé de mercure.

Une série de réactifs peut servir pour environ 15 échantillons selon la qualité des réactifs ou de la valeur des résultats obtenus. Lorsque l'enregistreur ne donne plus de signal, on doit changer les réactifs.

Lors de l'analyse on passe un sang de concentration connue à tous les 7 échantillons et à tous les changements de réactifs pour vérifier la stabilité du système.

Préparation de l'échantillon. (Mercure inorganique)

Procéder exactement tel que décrit précédemment, mais en utilisant $SnCl_2$ seul à la place du $SnCl_2$-$CdCl_2$.

Solution de $SnCl_2$ 10% (Fisher T-142): Préparer H_2SO_4 9N; ajouter 250 mL de H_2SO_4 concentré à environ 700 mL d'eau distillée et déminéralisée puis compléter à 1 litre. Dissoudre alors 10 g de $SnCl_2$ dans 25 mL de H_2SO_4 9N. Compléter à 100 mL avec de l'eau distillée et déminéralisée. (C'est la même solution que celle utilisée pour le mercure urinaire).

Mercure organique = Mercure total - Mercure inorganique.

Calculs.

Mesurer la hauteur des pics en mm. La concentration des inconnus est déterminée par comparaison avec la courbe d'étalonnage dans le sang. Déterminer la pente de la courbe d'étalonnage par moindre carrés sur ordinateur ou par une méthode graphique.

Calculer la concentration des inconnus par l'équation suivante:

$$\text{concentration } (\mu g/L) = \frac{\text{lecture (inconnu)}}{m}$$

Contrôle de qualité.

(Utiliser les deux contrôles internes: Hg bas et Hg élevé).

- BEHRING 1
- BEHRING 2
- Hg bas
- Hg élevé

BEHRING.

Matériel de référence provenant de l'Institut Behring (OSSD-21, OSSE-21).

Sang de boeuf hémolysé et lyophilisé, additionné de 1 mg d'EDTA par mL de sang comme anti-coagulant. Ils sont reconstitués et conservés dans des tubes Eppendorf de 1.5 mL en polypropylène (no. 22-36-411-1) et congelés à -80°C.

Hg bas, Hg élevé.

Contrôles internes constitués d'un pool de sang hépariné, valeurs connues. Ils sont conservés dans des tubes Eppendorf de 1.5 en polypropylène (no. 22-36-411-1) et congelés à -80°C pour une période permettant un contrôle adéquat (environ 2 ans).

La valeur de la pente doit demeurer sensiblement la même d'une fois à l'autre et le coefficient de corrélation doit être d'au moins 0.999. La valeur des contrôles doit se situer à l'intérieur de 2 écart-types de la valeur cible établie préalablement. Sinon, prendre les mesures appropriées.

Référer au cahier de contrôle de qualité et y inscrire les différentes coordonnées.

Références.

EBBESTADT V., GUNDERSON and TORGRIMSEN T.A.
Simple method for the determination of inorganic mercury and methylmercury in biological samples by flameless atomic absorption.
Atomic absorption newsletter 14(6), Nov-Dec 1977, 142-143.

Revisé: Octobre 1983, par Sylvie Rodrigue

Relu et approuvé par: Michel Lefebvre: Michel Lefebvre

Ghislaine Harvey: Ghislaine Harvey

J.-Philippe Weber: 84/02/10

Problèmes techniques - Mercure

La courbe ne se répète pas:

La durée de conservation de la courbe est pour le mercure sanguin environ 1 mois et le mercure urinaire environ 3 mois. Refaire un contrôle à concentration connue. Si la hauteur est satisfaisante, refaire une nouvelle courbe. Si la hauteur du contrôle n'est pas satisfaisante, il s'agit d'un problème du système.

Les contrôles n'atteignent pas une bonne hauteur:

Il s'agit probablement d'une fuite. Vérifier toute la tubulure, surtout les joints. On peut réparer une fuite en se servant de ruban de teflon.

Pics larges:

Il y a un mauvais débit du mercure dans la cellule. Changer l'anhydrone. Vérifier toute la tubulure pour que tous les tubes soient libres.

On ne peut faire que 15 analyses avec les mêmes réactifs:

Les réactifs sont vieux, les refaire.

Saturation de l'enregistreur:

Il y a présence de contamination. Il faut laisser circuler de l'air dans le système un certain temps. S'il y a encore saturation il y a un réactif qui est contaminé.

M-121-A

Centre de Toxicologie du Québec

DOSAGE DU PLOMB DANS LES CHEVEUX

Méthode révisée - août 1981

RÉSUMÉ

Les cheveux sont dissous dans l'acide nitrique concentré chaud. Les plomb est dosé par absorption atomique (four au graphite) en présence d'un modificateur de matrice, le nitrate d'ammonium.

MATÉRIEL

- Spectrophotomètre à absorption atomique Perkin-Elmer, modèle 5000, avec correcteur de bruit de fond ou deutérium.
- Four au graphite Perkin-Elmer, modèle 500, avec échantillonneur automatique AS-40.
- Tubes au graphite recouverts de carbone pyrolytique.
- Lampe EDL PLOMB - Perkin-Elmer.
- Micropipettes Eppendorf de 10, 200, 500 µL.
- Pipettes jetables de 1 et 10 mL.
- Tubes en polypropylène Falcon de 50 mL (B-D #2070).
- Godets jetables de 500µL ou 1 mL en polystyrène Fisher, #2-544-2 et 2-544-19.
- Fioles jaugées 100 mL.
- Bouteilles en Nalgène (1 L).

RÉACTIFS

- Acide nitrique concentré Baker #5-9063 "Suitable for mercury determination" (HNO_3).

- Eau déminéralisée et distillée (H_2O d + d).

- Acide nitrique 0.5% (HNO_3 0.5%)
  - ajouter 5 mL $HNO_{3(c)}$ à 1 L H_2O d + d

- Solution-mère de Pb 1000 mg/L Fisher SO-L-21.

- Solution-étalon A: 10 mg/L (10 ppm)
  - pipetter 1.0 mL de la solution-mère dans une fiole jaugée de 100 mL préalablement rincée avec HNO_3 0.5%
  - ajouter HNO_3 0.5% jusqu'au trait de jauge
  - bien mélanger
  - transférer dans une bouteille de Nalgène de 100 mL

- Solution-étalon B : 200 µg/L
  - pipetter 2.0 mL de la solution-étalon A dans une fiole jaugée de 100 mL préalablement rincée avec HNO_3 0.5%
  - compléter avec HNO_3 0.5% jusqu'au trait de jauge
  - bien mélanger
  - transférer dans une bouteille de Nalgène de 100 mL

.../3

RÉACTIFS (suite)

- Nitrate d'ammonium 4%
  - ajouter 2 g de NH_4NO_3 dans 50 mL de H_2O d + d
  - bien mélanger

PARAMÈTRES INSTRUMENTAUX

- Absorption atomique: Perkin-Elmer 5000

  Lampe : Pb EDL: puissance 10 W
  l'énergie doit être entre 67 et 70

  Longueur d'onde : 283.3 nm

  Fente : 0.7 nm (LOW)

  Correcteur : allumé

  Temps de lecture : 2.0 secondes

  Mode :
  - PEAK HT
  - ABS
  - AA/BG

- Four au graphite P.E.-500

  Tube : recouvert de carbone pyrolytique

.../4

Programme de températures : (peut être modifié selon conditions)

STEP	T (^0C)	Ramp	Hold	Read	Baseline	Int. Flow
1	130	5	20	-	-	-
2	350	10	2	-	-	-
3	600	2	8	-	-	-
4	600	1	6	-	4	50
5	2000	0	5	0	-	50
6	2700	1	4	-	-	-

Volume injecté : 20 µL (on peut baisser à 10, si nécessaire)

N.B. [Les caractéristiques des tubes en graphite pouvant] [varier d'un lot à l'autre, il faut vérifier pério-] [diquement le programme de températures, en parti-] [culier la température de carbonisation.]

.../5

PROTOCOLE

1) Préparation du cheveu:

L'échantillon de cheveux est coupé, lavé s'il y a lieu, pesé et digéré selon la méthode établie (voir "Préparation des cheveux pour dosage des métaux", révision août 1981).

La solution finale (digérat) contient les cheveux digérés (environ 10 mg) dans un volume total de 1.0 mL de HNO_3 50%.

2) Dosage:

Le dosage se fait par la méthode d'ajouts dosés plutôt que par une courbe étalon, les digérats de cheveux ne donnant pas le même facteur de réponse que la matrice aqueuse.

Dans des godets de 500 µL, ajouter successivement:

A: échantillon seul - 100 µL de digérat de cheveu
- 100 µL de H_2O
- 200 µL de NH_4NO_3 4%

B: échantillon + ajout- 100 µL de digérat de cheveu
- 100 µL de solution-étalon B (200 µg/L)
- 200 µL de NH_4NO_3 4%

- Bien mélanger

- Préparer également un blanc réactif de Pb dans HNO_3 50%: dans du tube de 12 x 75: 500 µL H_2O
500 µL HNO_3 concentré

- Le blanc réactif est digéré et dosé comme les échantillons.

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Contrôle de qualité:

Contrôler les résultats en dosant une solution témoin de cheveux à concentration connue. Les solutions contiennent des cheveux digérés dans une matrice de HNO_3 50%, ainsi qu'une certaine quantité de plomb ajouté:

Solution-témoin	Concentration (µg/g)
BAS	3
MOYEN	Bas +25
HAUT	Bas +50

Calculs:

Les calculs se font en tenant compte de l'effet matrice de chaque digérat. Comme le Pb du blanc réactif sera probablement mieux atomisé que celui des échantillons, il est important de calculer la concentration de Pb à soustraire de l'échantillon et de ne pas soustraire directement la hauteur du pic du blanc.

(a) Conc. du blanc (en solution) (µg/L)

$$C\ BLANC = \frac{\text{lecture blanc}}{\text{lecture (blanc + ajout) - lecture blanc}} \times 200\,\mu g/L$$

(b) Conc. de l'échantillon (en solution) [µg/L]

$$C\ ech = \frac{\text{(lecture A}}{\text{(lecture B - lecture A}} \times 200\ \ g/L) - C\ BLANC$$

.../7

Calculs (suite)

(c) Conc. de l'échantillon (dans les cheveux) [µg/g]

$$\text{C cheveux} = \frac{\text{C ech} \quad (\mu g/L)}{\text{POIDS CHEVEUX (mg)}} \times \text{volume du digérat (en mL)}$$

N.B. Le volume du digérat est normalement de 1 mL.

- On peut également utiliser le programme AJOUTCHEVEU dans le bloc STATS, sur le IBM PC-XT.

Centre de Toxicologie du Québec

DOSAGE DE SELENIUM DANS LES CHEVEUX

Domaine d'application

Cette méthode permet de doser le sélénium dans les cheveux. La limite de détection dépend de la quantité de cheveux disponible. Pour un échantillon de 20 mg, elle est de l'ordre de 0.05 µg/g.

Principe et théorie

Identique au sélénium urinaire et sanguin.

Matériel

Identique au sélénium sanguin et urinaire, plus:

- Gabarit pour couper les cheveux en segments de 1 cm.
- Balance analytique précise à ± 0.1 mg (Sartorius).
- Fioles à scintillation en plastique New England Nuclear pour conserver les segments de cheveux.

Réactifs

Identiques à la méthode décrite pour le sang et l'urine, sauf :

- Solution étalon 2 µg/ml Se:

  200 µl de la solution mère dans une fiole jaugée de 100 ml H_2O.

Protocole

Paramètres du spectrophotomètre et du four au graphite: identiques à ceux du sélénium sanguin et urinaire.

Manipulation:

Inconnu:

- Peser avec une précision de 0.1 mg environ 20 mg de cheveux dans un tube à bouchon vissant.
- Ajouter 200 µl de HNO_3 conc., sceller le tube et faire chauffer au bain-marie à 80°C pendant une heure.
- Refroidir dans la glace.
- Ajouter 200 µl de Ni 2% et bien mélanger.
- Verser dans un godet de polystyrène.
- Lire à l'absorption atomique.

Etalons:

- Déterminer la teneur en sélénium d'un blanc réactif.

- Faire une courbe d'étalonnage en ajoutant des quantités de sélénium équivalentes à 1 µg/g et 2 µg/g.
- Peser précisément 3 fois 20.0 mg du même cheveu.
- Ajouter respectivement 0, 10 et 20 µl de la solution étalon à chaque échantillon.
- Traiter comme les inconnus.

Calculs

Déterminer la pente de la courbe étalon en prenant

pour abcisse 0 20 40 ng

et ordonnée h_o, h_{10}, et h_{20} mm

Déterminer la concentration des inconnus par la formule suivante:

$$\text{conc.}\ \left(\frac{\mu g}{g}\right) = \frac{(\text{h inconnu} - \text{h blanc réactif})\ \text{mm}}{\text{pente}\ \frac{\text{mm}}{\text{ng}} \times \text{poids cheveux (mg)}}$$

Dr Jean-Philippe Weber, Chim.P.
Responsable, Toxicologie industrielle
Centre Régional de Toxicologie

Mai 1979

Appendix 8.1.1/2

DETAILED LABORATORY METHODS

MAYO CLINIC LABORATORIES, ROCHESTER, MINNESOTA

TEST: HAIR AND NAIL FOR TRACE METAL ANALYSIS

REFERENCE

The "use" and "misuse" of human hair in trace metal analysis: H. Shy-Peck and B. Joseph, In Chemical Toxicology and Clinical Chemistry of Metals (S. S. Brown and J. Savory, eds.). Academic Press, New York, 1983, pp. 159-163.

PRINCIPLE OF METHOD

Samples of hair or nails are washed with a dilute solution of Triton X-100 to remove surface metal contaminants followed by rinsing with double glass distilled water, isopropanol, and then air dried. Drying in an oven is not done to avoid loss of volatile selenium and mercury. When dry, the sample is weighed (0.1-0.2 g) and placed in a sealed Teflon coated digestion bomb. Nitric acid is added to solubilize the sample. Analysis of the digested sample is performed according to the standard procedures listed elsewhere.

COLLECTION AND HANDLING OF SPECIMENS

Hair cut from the nape of the neck, occipital area, pubic area or the clippings from the end of the finger or toe nail can be analyzed. At least 0.5 g of specimen should be collected. Hair collected from subjects that is longer than 3 inches should have the end (oldest growth) removed to a length no longer than 3 inches from the root end.

EQUIPMENT

1. Cahn Electrobalance - use for small samples (less than 0.1 g). Weigh to 5 decimal places.
2. Sartorius 5-place balance - use for samples larger than 0.1 g. Weigh to 4 decimal places.
3. Ashless filter paper.
4. Digestion bomb - SAVILLEX, Minneapolis, Minnesota - ½ oz (15 cc)

REAGENTS

1. Double glass distilled water, store in polypropylene carbouy.
2. Triton X-100, 0.1%. Using high purity Triton X-100, dilute 1 mL with 1 liter of double glass distilled water. This reagent must be checked for background trace elements prior to use.
3. Isopropanol. Double glass distilled from Burdick and Jackson.
4. Sub-boiling redistilled concentrated nitric acid.

PROCEDURE

1. Place the hair or nail sample (approximate weight 0.1-0.2 g) on the vacuum filter unit with filter paper in place.

2. Rinse three (3) times with 0.1% Triton X-100 (10 mL each time). Remove all traces of liquid by vacuum.
3. Rinse the sample three (3) times with distilled water (10 mL each time) removing excess by vacuum.
4. Rinse with 10 mL of distilled isopropanol removing excess by vacuum.
5. Using a forceps, remove the sample and filter paper and place on the lab bench under the HEPA filter hood to dry.
6. When dry, weigh the sample.
7. Transfer to the digestion bomb and add 1 mL of redistilled concentrated nitric acid. Seal the digestion bomb.
8. Place digestion bomb in the heating block at 120°C until entire sample is dissolved (approximately one hour).
9. Cool to room temperature before opening.
10. Remove an aliquot for analysis according to the specific procedures outlined elsewhere

Thomas P. Moyer, Ph.D.
May 9, 1985

TEST: ARSENIC (SERUM, URINE, WHOLE BLOOD, HAIR AND NAILS)

REFERENCE

Analytical Methods for Atomic Absorption Spectroscopy using the HGA Graphite Furnace. Perkin-Elmer Corporation, Norwalk, Connecticut, 1980.

(See General Reference for Analyses by Atomic Absorption and Atomic Emission Spectroscopy.)

PRINCIPLE OF METHOD

A flameless atomic absorption spectrometric method is employed using a carbon rod atomizer. The carbon rod atomizer, or furnace, is placed in the light path from the electrodeless discharge lamp instead of the usual air-acetylene burner. When sufficient current is applied to this carbon rod, the temperature will rise from ambient to 2700 in less than 6 seconds, effectively atomizing the elements in the sample placed inside the rod. As with the flame atomic absorption procedure, quantitation is accomplished by measuring the absorbance of the arsenic resonance line (193.7 nm) from the electrodeless discharge lamp.

PATIENT PREPARATION

None.

COLLECTION AND HANDLING OF SPECIMENS

Acid-washed containers (preferably Teflon) must be used for all specimens.

ADEQUACY OF SPECIMEN

A minimum of 5 mL of urine is needed, an aliquot from a full 24-hour collection; 2 mL of serum, or 0.5 g hair and nails.

EQUIPMENT

A reliable double beam atomic absorption spectrophotometer equipped with a carbon rod atomizer and the necessary power supply is used for these determinations. For the procedure described here, a Perkin-Elmer Model 5000 atomic absorption spectrophotometer is used in conjunction with the Model HGA500 graphite furnace. A pre-cut graphite platform is positioned in the carbon rod so that 20 µL samples are reproductively deposited on the platform. The platform technique produces higher sensitivity for arsenic over the regular carbon rod method.

REAGENTS

1. Nitric acid. The commercial concentrated nitric acid is redistilled by Central Services into acid-washed Teflon containers. This acid in turn is redistilled by sub-boiling distillation into clean Teflon containers and so labeled.

2. 0.1% Triton X-100 in 10% redistilled HNO_3. Pour 100 mL of the concentrated, Teflon redistilled HNO_3, and pipet 1.0 mL of Triton X-100

into an acid-washed liter volumetric flask and bring to volume with redistilled H_2O.

3. Nickel nitrate ($NiNO_3$). Dissolve 4.9532 g $(NiNO_3)_2 \cdot 6H_2O$ of high purity into one liter of 10% HNO_3 for 1000 PPM Ni.

4. Stock standard. This is a commercially available certified atomic absorption reference solution containing 1000 µg/mL of arsenic.

5. Working stock standard. 1 mL of the 1000 µg/mL commercially available stock arsenic standard is pipetted into an acid-washed 100 mL volumetric flask. Add 2.0 mL concentrated redistilled nitric acid and make to volume with distilled water. This provides a working stock standard containing 10 µg/mL.

6. Working standard. Pipet 2 mL of the 10 µg/mL working stock standard and 2.0 mL redistilled concentrated HNO_3 into a 100 mL volumetric flask that has been acid-washed. Bring to volume with redistilled water. This gives a working standard of 200 ng/mL.

PROCEDURE

1. Instrument Parameters:

	Temp	Ramp	Hold	
Dry	200°	25	15	
	250°	1	10	
Char	1000°	1	20	
Atomize	2400°	0	6	Record (-5) Read (0) Int. Flow (20 cc/min)
Cool	20°	1	14	

P.E. L'vov Platform
20 µL injection

2. Sample Preparation:

The standard curve is established by the standard addition procedure. Zero (0.0), one-tenth (0.1), two-tenths (0.2), three-tenths (0.3), and four-tenths (0.4) mL of the 200 ng/mL standard is added to 12x75 Sarstedt plastic test tubes. To these add 0.2 mL of a low or normal (As content) urine for a matrix like the unknowns. Then add 0.8 (blank), 0.7, 0.6, 0.5, 0.4 mL of the 0.1% Triton X-100 in 10% HNO_3 solution. Then add 1.0 mL of the 1000 PPM $NiNO_3$ solution to each Sarstedt test tube. Mix, pour into cups, and run standard curve.

Urine samples - Place 0.2 mL urine in 12x75 Sarstedt plastic tubes. Add 0.8 mL of 0.1% Triton X-100 in 10% HNO_3 followed by 1.0 mL $(NiNO_3)_2 \cdot 6H_2O$ in 10% HNO_3. Mix, pour into cups and analyze.

Serum samples - Place 0.2 mL serum in 12x75 Sarstedt plastic tubes. Add 0.8 ml 0.1% Triton X-100 in 10% HNO_3 (a ppt will form). Mix well, add 1.0 mL 1000 PPM $(NiNO_3)_2 \cdot 6H_2O$ in 10% HNO_3 solution. Mix and centrifuge. Pour supernatant into cups and analyze.

Hair and nail samples - Follow the digestion procedure. Of this digestion, place 0.2 mL into 12x75 Sarstedt test tube, 0.8 mL 0.1% Triton X-100 in 10% HNO_3 solution, mix, pour into cups, and analyze.

	Blank	10 ng/mL	20 ng/mL	30 ng/mL	40 ng/mL	Control	Sample
Specimen	0	0	0	0	0	0	0.2
Matrix	0.2	0.2	0.2	0.2	0.2	0	0
Control	0	0	0	0	0	0.2	0
Std. 200 ng/mL	0	0.1	0.2	0.3	0.4	0	0
.1% Tr X-100 in 10% HNO_3	0.8	0.7	0.6	0.5	0.4	0.8	0.8
1000 PPM $NiNO_3$	1.0	1.0	1.0	1.0	1.0	1.0	1.0
	2.0	2.0	2.0	2.0	2.0	2.0	2.0

Mix, pour into cups and analyze.

CALCULATIONS

Absorbance values for specimens are compared to standard curve prepared from absorbance values for standards. In order to determine the value for 24-hour urine excretion, the dilution factors and total volume must be used.

CRITERIA FOR RESULTS

Serum	<0.07	µg/mL;	panic	>0.15	µg/mL
Urine	<25	µg/24 hrs;	panic	>150	µg/24 hrs
Hair/nails	<1	µg/g;	panic	>10	µg/g

T. Moyer

Thomas P. Moyer, Ph.D.
2/15/82
Revised 3/2/83
Revised 10/5/83
Revised 11/16/84
Revised 5/9/85

TEST: CADMIUM (BLOOD, URINE, HAIR AND NAILS)

REFERENCE

Revision of Analytical Methods for Atomic Absorption Spectrophotometry. Perkin-Elmer Corporation, Norwalk, Connecticut, 1980.

(See General References for Analysis by Atomic Absorption and Atomic Emission Spectroscopy.)

PRINCIPLE OF METHOD

A flameless atomic absorption spectrometric method is employed using a carbon rod atomizer. The carbon rod atomizer, or furnace, is placed in the light path from a hollow cathode lamp. When sufficient current is applied to this carbon rod, the temperature will rise from ambient to 2700°C in less than 6 seconds, effectively atomizing the elements in the samples placed inside the rod. Quantitation is accomplished by measuring the absorbance of the cadmium resonance line (228.8 nm) from the hollow cathode lamp.

PATIENT PREPARATION

None.

COLLECTION AND HANDLING OF SPECIMENS

It is essential that blood specimens be collected in acid-washed containers (See the blood collection procedure). Urine should be collected in an acid-washed polypropylene bottle. Collection of hair and nails is defined in the Hair and Nails Procedure.

ADEQUACY OF SPECIMEN

A minimum of 1 mL of whole blood and 5 mL urine is necessary. 0.5 g of hair or nails are required for analysis.

EQUIPMENT

A reliable double beam atomic absorption spectrophotometer equipped with a carbon rod atomizer and the necessary power supply is used for these determinations. For the procedure described here, a Perkin-Elmer Model 5000 atomic absorption spectrophotometer is used in conjunction with the Model HGA500 graphite furnace. A pre-cut graphite platform is positioned in the carbon rod so that 20 µL samples are reproductively deposited on the platform. The platform technique produces higher sensitivity for cadmium over the regular carbon rod method.

REAGENTS

1. Concentrated redistilled HNO_3.

2. Stock cadmium standard. This standard commercially available certified atomic absorption reference standard containing 1000 µg/mL.

3. Working stock standard. 1 mL of the 1000 µg/mL commercially available stock cadmium standard is pipetted into an acid-washed 250 mL volumetric

flask. Add 2.0 mL concentrated redistilled nitric acid and make to volume with redistilled water. This provides a working stock standard containing 4 µg/mL.

4. Working standard. Pipet 0.5 mL of 4 µg/mL cadmium working stock standard into a 200 mL acid-washed flask. Add 2 mL concentrated redistilled HNO_3 and make to volume with redistilled water. This gives 10 ng/mL. This standard should be made fresh with each batch of analyses.

PROCEDURE

1. Instrument Parameters:

	Temp	Ramp	Hold	
Dry	170°	10	20	
Char	230°	5	40	
Atomize	2100°	1	3	Read Int. flow (20 cc/min)
Clean	2700°	1	2	
Cool	20°	1	14	

P.E. L'vov Platform
20 µL injection

2. Sample Preparation:

The standard curve is established by a standard addition procedure. One-tenth (0.1), two-tenths (0.2), and three-tenths (0.3) mL of 10 ng/mL standard is added to separate 15x160 nm acid-washed Teflon tubes. To each blank and standard, 0.5 mL of a low cadmium concentration urine is added for matrix similarity. Then 0.5 mL of concentrated redistilled HNO_3 is added and heated for 10 minutes to allow foaming. After all foaming has subsided, 0.5 mL of H_2O_2 is added and heated for an additional 10 minutes to complete digestion.

After cooling of the digest, add 0.5 mL of redistilled water to make a total volume of 2.0 mL. Controls and unknowns follow the same digestion procedure as is outlined below. A reagent blank is also run in the same manner using distilled water instead of urine.

	BlK	1 ng	2 ng	3 ng	R.BLK	Control	Unknown
Specimen	0	0	0	0	0	0	0.5
Urine matrix	0.5	0.5	0.5	0.5	0	0	0
Std. (10 ng/mL)	0	0.1	0.2	0.3	0	0	0
Control	0	0	0	0	0	0.5	0
Conc. HNO_3	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Heat 10 minutes.							
H_2O_2	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Heat 10 minutes, then cool.							
H_2O	0.5	0.4	0.3	0.2	1.0	0.5	0.5
TV.	2.0	2.0	2.0	2.0	2.0	2.0	2.0

Mix, pour into cups and analyze.

CALCULATIONS

Absorbance values for specimens are compared to standard curve prepared for absorbance values for standards. In order to determine the value for 24-hour urine excretion, the dilution factor and total volume must be used.

If standards are plotted as ng concentration/2 mL total volume of sample digested, multiply concentration times 2 because 0.5 mL of sample was digested.

Examples:

Whole blood:

$$\text{A unknown} - \text{A reagent blank} \times \frac{1}{\text{slope}} \times 2 = \text{ng/mL}$$

Urine:

$$\text{A unknown} - \text{A reagent blank} \times \frac{1}{\text{slope}} \times 2 \times \text{volume in liters} = \mu\text{g/24 hr}$$

Hair or Nails:

$$\text{A unknown} - \text{A reagent blank} \times \frac{1}{\text{slope}} \times 2 \times \frac{\text{total volume of digest}}{0.5} \div \text{hair weight} = \text{ng/g}$$

CRITERIA OF RESULTS

Specimen	Normal	Panic
Whole blood	<5 ng/mL	>50 ng/mL
Urine	<3 µg/24 hr	>50 µg/24 hr
Hair	Not established at Mayo Clinic	

Thomas P. Moyer, Ph.D.
3/26/82
Revised 3/9/83
Revised 5/9/85

TEST: LEAD (BLOOD, HAIR AND NAILS)

REFERENCE

Fernandez, F. J.: Micromethod for lead determination on whole blood by atomic absorption with use of the graphite furnace. Clin. Chem. 21, 558-561, 1975.

(See General References for Analyses by Atomic Absorption and Atomic Emission Spectroscopy.)

METHOD

A flameless atomic absorption spectrometric method is employed using a carbon rod atomizer. The carbon rod atomizer, or furnace, is placed in the light path from the hollow cathode lamp instead of the usual air-acetylene burner. When sufficient current is applied to this carbon rod, the temperature will rise from ambient to as much as 2700°C in less than 6 seconds, effectively atomizing the elements in the samples placed inside the rod. As with the flame atomic absorption procedures, quantitation is accomplished by measuring the absorbance of the lead resonance line (283.2 nm) from the hollow cathode lamp which is directly proportional to the concentration of lead in the sample placed in the carbon rod. The readings are displayed by readout system of the 5000 atomic absorption.

PATIENT PREPARATION

None.

COLLECTION AND HANDLING OF SPECIMENS

The best method for collecting the blood specimen is to use an acid-washed Sarstedt syringe containing EDTA as the anticoagulant.

Specimen collection for hair and nails is defined in the Hair and Nails Procedure.

ADEQUACY OF SPECIMENS

A 1 mL volume of whole blood is needed for the determination. After the specimen is thoroughly mixed with the anticoagulant, it may be transported to the laboratory without refrigeration and may be stored frozen in a tightly stoppered container for an indefinite period.

EQUIPMENT

A reliable double beam atomic absorption spectrometer equipped with a carbon rod atomizer and the necessary power supply is used for these determinations. For the procedure described here, a Perkin-Elmer Model 5000 atomic absorption spectrometer is used in conjunction with the model HGA500 graphite furnace.

REAGENTS

1. Stock lead standard. This standard commercially available certified atomic absorption reference standard containing 1000 µg/mL lead.

2. Working stock standard. The standard containing 10 µg/mL is prepared by pipetting 1 mL of the stock standard into an acid-washed 100 mL volumetric flask. Add 2 mL redistilled concentrated HNO_3 and bring to volume with redistilled water.

3. Working standard. These standards are prepared by pipetting 1, 2, 3 and 4 mL of the 10 µg/mL working stock standard into individually acid-washed 100 mL volumetric flasks. Add 2 mL redistilled concentrated HNO_3 and bring to volume with redistilled water. These standards will contain 100, 200, 300, and 400 ng/mL, and when diluted by the same procedure as used for specimens will give final concentrations of 20, 40, 60 and 80 ng/mL.

4. Diluent. 1 mL Triton X-100 is pipetted into a liter volumetric flask and made to volume with distilled water.

5. Quality Control. Reconstitute with 5 mL of redistilled water a New York State Health Department freeze-dried cow blood.

PROCEDURE

1. Instrument parameters:

   Drying temperatures of 120°C (ramp time of 20 sec and hold time of 20 sec), charring temperature of 400°C (ramp time of 20 sec and hold time of 20 sec), and atomization temperature of 2500°C (ramp time of 1 sec and hold time of 5 sec) are used. The argon flow is adjusted to 20 cc/min at atomization and background deuterium correction is used.

2. Sample preparation:

   Each standard, control, and specimen is diluted 1-5 with a 0.1% solution of Triton X-100 by a pre-calibrated Hamilton digital dilutor. Each is diluted into 2 mL volume flat-bottom autoanalyzer sample cup, and placed onto round racks for AS-40 sampler. The AS-40 sampler places 10 µL of diluted sample into carbon rod and the concentration of lead is determined by comparing absorbance values obtained from samples to absorbances of working standards.

CALCULATION

Since standards, controls, and specimens are diluted and analyzed by the same method, concentrations in µg/mL can be directly obtained from the absorbances of blank and standards plotted against their concentrations of 0, 0.1, 0.2, 0.3, and 0.4 µg/mL. If a dilution other than 1-5 is required, then the subsequent dilution factor must be used for the calculation.

Hair or nail concentration is then corrected for the fraction of the digested sample used, divided by the sample weight in grams, and reported as µg/g.

INTERPRETATION OF RESULTS

Specimen	Normal	Panic
Blood	< 0.2 μg/mL*	> 0.6
Hair and Nails	<25 μg/g	>25 μg/g

PANIC VALUES

Results greater than the panic values listed above should be immediately telephoned to the physician.

T. Moyer

Thomas P. Moyer, Ph.D.
10/11/83
Revised 5/9/85

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* Note: The Department of Occupational Safety and Health Act and the World Health Organization consider results <0.4 μg/mL to be normal. Our range applies to nonexposed rural patients.

TEST: MERCURY (BLOOD, SERUM, URINE, HAIR AND NAILS)

REFERENCES

Stainton, M. P.: Syringe procedure for transfer of nanogram quantities of mercury vapor for flameless atomic absorption spectrophotometry. Anal. Chem. 43:625-627, 1971.

METHOD

Mercury in an aqueous acid solution is oxidized with permanganate, to free any chemical bonded atoms, and a reducing agent (stannous chloride) is added to the solution to reduce the mercury to the volatile diatomic state. The vapor stage over the solution which is saturated with the atomic mercury is then injected into a borosilicate cell with quartz windows replacing the flame burner on an atomic absorption spectrophotometer. The mercury resonance line, 253.6 nm, emitted from the hollow cathode lamp passes through the borosilicate cell and is absorbed by the mercury atoms at ground state. The absorbance of this resonance line by the mercury atoms is directly proportional to the concentration of mercury atoms in the vapor.

PATIENT PREPARATION

None.

COLLECTION AND HANDLING OF SPECIMENS

Blood specimens should be collected in a heparinized tube. If a metal chelating anticoagulant, such as EDTA, is used instead of heparin, it must be checked to be sure it is mercury-free before using. When a serum specimen is removed from cells it should be put into an acid-washed serum tube.

Urine must be collected in an acid-washed bottle and a full 24-hour collection should be made.

Hair and nail collection procedure is defined in the Hair and Nail Procedure.

ADEQUACY OF SPECIMEN

A minimum of 3 mL of blood, serum or urine is adequate for the test. The urine specimen should be a representative aliquot of the full 24-hour collection. Any of the specimen may be stored for an indefinite period in the frozen state in a tightly stoppered container. 0.5 g of hair or nail are required for analysis.

EQUIPMENT

A reliable double beam atomic absorption spectrometer may be used for this determination. A background correction is desirable. A quartz cell, 1 cm in diameter x 11 cm in length, equipped with quartz windows replaces the conventional flame burner for the atomic absorption spectrometer. The cell is equipped with a 5 mm inlet tube at one end and a capillary exit tube at the other end. The cell is mounted on the burner assembly in such a way that the light beam emitted from the hollow cathode lamp is focused directly on through the middle of the cell.

Twenty mL glass syringes with Teflon stoppers instead of needles are used as the reaction vessels.

REAGENTS

1. Concentrated sulfuric acid. Reagent grades of sulfuric acid are used without further purification.
2. Concentrated nitric acid. Reagent grades are used without further purification.
3. Digestion mix. In a clean 1000 mL glass flask, put 500 mL of distilled water and add 250 mL of concentrated sulfuric acid, very slowly and carefully, with constant agitation in order to reduce over-heating. Cool this solution and add 250 mL of concentrated nitric acid.
4. 5% $KMnO_4$. Dissolve 15.0 g of $KMnO_4$ in 300 mL distilled water.
5. 4% H_2SO_4. Add 20 mL H_2SO_4 to 480 mL of distilled water in a clean bottle and mix.
6. Reducing agent. Add 10 g of fresh stannous chloride ($SnCl_2$) to a 25 mL flask. Make to volume with 4% H_2SO_4 and mix well.
7. Diluent. Add 0.5 grams analytical grade $K_2Cr_2O_7$ and 20.0 mL of HNO_3 to a clean one liter volumetric flask and dilute to volume with distilled water. Store in polyethylene bottle in refrigerator.
8. Stock mercury standard. This is a commercially available certified atomic absorption standard reference solution containing 1.000 mg/mL of mercury.
9. Working stock standard. This is prepared by pipetting 1 mL of the stock standard into a one liter volumetric flask. Add 0.5 grams analytical grade potassium dichromate (0.05% by weight $K_2Cr_2O_7$) and 20.0 mL concentrated HNO_3. Bring to volume with distilled water, and store in polyethylene bottle in refrigerator.
10. Working standard. This standard is prepared by pipetting 0.25 mL of the working standard into a 25 mL volumetric flask and dilute to volume with diluent. This must be made fresh weekly.
11. Mercury control standard. 5 mL aliquots of a normal urine are put in clean tubes, tightly stoppered, and frozen. One of the control standards are thawed, thoroughly mixed and analyzed with each series of mercury analysis done.

PROCEDURE

1. Instrument.

The Perkin-Elmer 303 wavelength is set to 253.7 nm. Background is balanced by variation of the deuterium arc power supply.

2. Procedure.

To each of 3 acid-washed 20 mL stoppered, glass syringes, add 2 mL of the digestion solution, 0.5 mL of the 5% $KMnO_4$ solution, and either 0, 0.5, or 1.0 mL of the working standard and 1, 0.5, or 0 mL of diluent to the individual syringes. Insert the plunger and invert the syringe. Remove the stopper and expel the air from the syringe. Replace the stopper and mix thoroughly on a Vortex shaker. Remove the stopper and add 1 mL of the stannous chloride solution through the tip of the syringe, adjust the plunger to include a 9 mL air volume over the solution, replace the stopper, and mix thoroughly on the Vortex mixer. The 9 mL volume of vapor is injected into the quartz cell and the difference in absorbance readings are measured. A standard curve is prepared by using the 0 standard as the base line and plotting the 5 ng/mL and 10 ng/mL standards. Sample, specimens and the control samples are analyzed in the same way. One mL of urine, 1 mL of a 1 to 10 dilution of each whole blood or serum, or 1 mL of a 1 to 10 dilution of hair or nail digestion medium is used. Concentrations are obtained from the calibration curve by comparing the absorbance difference measured on the spectrometer.

CALCULATIONS

Since the volumes of the standards, the control standards, and the specimens are all 1 mL, the concentrations of the unknowns can be read directly from the calibration curve. The concentrations of blood specimens are multiplied x 10 and reported in µg/mL. The concentrations obtained for the urine specimens are multiplied by the volume of the 24-hour collection and are reported as µg/24-hour of specimen. Hair and nail results are multiplied x 10, divided by the weight in grams, and reported as µg/g.

NORMAL VALUES

Specimen	Normal		Panic	
Blood	< 0.005	µg/mL	> 0.05	µg/mL
Urine	<20	µg/24 hr	>50	µg/24 hr
Hair or Nail	< 1	µg/g	> 5	µg/g

CRITERIA FOR IMMEDIATE NOTIFICATION OF RESULTS

The requesting physician should be notified whenever the values are greater than the panic value.

REMARKS

None.

T. Moyer

Thomas P. Moyer, Ph.D.
1/11/81
Revised 7/11/84
Revised 5/9/85

TEST: SELENIUM (SERUM, URINE, HAIR AND NAILS)

REFERENCE:

Analytical Methods for Atomic Absorption Spectroscopy using the HGA Graphite Furnace. Perkin-Elmer Corporation, Norwalk, Connecticut, 1980.

(See General Reference for Analysis by Atomic Absorption and Atomic Emission Spectroscopy.)

Thompson, D. D. and Allen, R. J., Rapid determination of selenium in nutritional supplements by a flameless atomic absorption technique using a novel sample preparation. Atomic Spectros. 2, 53-58, 1981.

PRINCIPLE OF METHOD

The concentration of selenium in biological fluids is measured by flameless atomic absorption spectrometry using Zeeman background correction. An appropriate aliquot of sample solution is placed in a graphite tube, or furnace, where it is dried, ashed and atomized through programmed temperature increases. Quantitation is accomplished by measuring the absorbance of the selenium resonance line (196.0 nm) from an electrodeless discharge lamp.

Selenium is easily volatilized at elevated temperatures, particularly in the reduced state, and care must be taken to prevent premature volatilization during the drying and ashing steps of the graphite furnace program. In order to prevent loss of selenium, nickel ion is added to the test solution as a matrix modifier which forms a stable nickel selenide, a complex which will not volatilize at temperatures up to 1100°C.

PATIENT PREPARATION

None

COLLECTION AND HANDLING OF SPECIMENS

Acid-washed "Mayo metal-free" blood collection and storage containers must be used for serum specimens. See the collection instructions for each type of specimen.

ADEQUACY OF SPECIMEN

A minimum of 5 mL of urine is needed (an aliquot from a full 24-hour collection), 1 mL of serum, 0.5 g hair or nails.

EQUIPMENT

A reliable double beam atomic absorption spectrophotometer equipped with a graphite tube atomizer and the necessary power supply is used for these determinations. For the procedure described here, a Perkin-Elmer Model 5000 atomic absorption spectrophotometer is used in conjunction with the Model HGA 500 graphite furnace. A pre-cut graphite platform is positioned in the furnace so that 20 µL samples are reproducibly deposited on the platform. The platform technique produces higher sensitivity for selenium than the regular graphite furnace method.

REAGENTS

1. Nitric acid. Commercial concentrated nitric acid should be redistilled by Central Services into acid-washed Teflon containers. This acid, in turn, is redistilled by sub-boiling distillation into clean Teflon containers and so labeled.

2. Stock standard. This is commercially available as a certified atomic absorption reference solution containing 1000 μg/mL selenium.

3. Working stock standard. Pipet 1 mL of the 1000 μg/mL stock standard into an acid-washed 100 mL volumetric flask and bring to volume with 0.2% Triton X-100 and magnesium nitrate diluent. This gives 10 μg/mL.

4. Working standard. Pipet 1 mL of the 10 μg/mL working stock standard into an acid-leached 100 mL volumetric flask and bring to volume with 0.2% Triton X-100 and magnesium nitrate diluent. This gives 100 ng/mL.

5. Magnesium nitrate (1.4 g/L) in 0.2% Triton X-100. Pipette from an acid-leached pipette 2 mL of Triton X-100 surfactant into an acid-leached Teflon one liter container. To this, add 1.4 g magnesium nitrate hexahydrate, 99.999%, Gold Label (ALDRICH), and bring to volume with redistilled water.

6. Nickel nitrate, magnesium nitrate, and Triton X-100 diluent. Pipette from an acid-leached pipette 2 mL of Triton X-100 surfactant into an acid-leached Teflon one liter container. To this, add 1.4 g magnesium nitrate hexahydrate, 99.999%, Gold Label (ALDRICH), 9.9064 g nickel nitrate hexahydrate, 99.999%, Gold Label (ALDRICH) for 2000 PPM Ni, and bring to volume with redistilled water.

PROCEDURE

1. Instrument Parameters:

	Temp	Ramp	Hold		
Dry	160°	25	15		
	250°	1	10		
Char	800°	1	40		
Atomize	2400°	0	6	Record	(-5)
				Read	(0)
				Int. Flow	(0)

P.E. L'vov Platform
20 μL injection

2. Sample Preparation:

The standard curve is established by the following procedure. Zero (0.0), one-tenth (0.1), two-tenths (0.2), three-tenths (0.3), and four-tenths (0.4) mL of the 100 ng/mL selenium standard is pipetted into 12x75 Sarstedt plastic test tubes, followed by 0.2 mL of a low concentration urine for matrix. To these, add 0.8, 0.7, 0.6, 0.5, and 0.4 mL of the 0.2% Triton X-100 and magnesium nitrate diluent. Then add 1 mL of the nickel nitrate, magnesium nitrate, and 0.2% Triton X-100 diluent. Mix, pour into sample cups and analyze. Establish standard curve using absorbance vs. concentration values.

Serum samples: Place 0.2 mL serum in 12x75 Sarstedt plastic tubes. Add 0.8 mL 0.2% Triton X-100 and magnesium nitrate diluent and 1 mL nickel nitrate, magnesium nitrate, and 0.2% Triton X-100 diluent. Mix well, pour into sample cups and analyze.

Urine samples: Do the same as serum.

Hair, nails, and other tissues: Samples are prepared according to the hair and nail preparation procedure. 0.2 mL of the digested hair sample is placed into a 12x75 Sarstedt test tube. 0.8 mL 0.2% Triton X-100 and magnesium nitrate diluent, and 1 mL nickel nitrate, magnesium nitrate, 0.2% Triton X-100 diluent are added, mixed, poured into sample cups and analyzed.

		ng/mL					
	Blk	5	10	15	20	Control	Sample
Matrix	0.2	0.2	0.2	0.2	0.2	0	0
Specimen	0	0	0	0	0	0	0.2
Control	0	0	0	0	0	0.2	0
Std. 100 ng/mL	0	0.1	0.2	0.3	0.4	0	0
0.2% Tr X-100 in $Mg(NO_3)_2$	0.8	0.7	0.6	0.5	0.4	0.8	0.8
$Ni(NO_3)_2$, $Mg(NO_3)_2$ and 0.2% Tr X-100	1.0	1.0	1.0	1.0	1.0	1.0	1.0
	2.0 mL	2.0	2.0	2.0	2.0	2.0	2.0

CALCULATIONS

Absorbance values for specimens are compared to standard curve prepared from absorbance values for standards. In order to determine the value for 24-hour urine excretion, the dilution factors and total volume must be used. Hair and nail concentrations are corrected for dilution, divided by total hair weight and reported as ng/g.

NORMAL VALUES

	Normal	Panic
Serum	85-125 ng/mL	<25 or >150
Urine	0-35 µg/24 hours	>50
Hair or Nails	Normals not established at Mayo Clinic	

CRITERIA FOR IMMEDIATE NOTIFICATION OF RESULTS

Serum concentrations of selenium greater than 140 ng/mL should be reported immediately. Concentrations of selenium in serum less than the established normal range do not require immediate notification of results. Patients maintained on partial or total parenteral nutrition may have serum concentrations less than 5 ng/mL for relatively long periods.

REMARKS

Selenium is easily reduced to the elemental state if allowed to stand at room temperature in solutions of organic matrices. In order to avoid loss of selenium in samples by reduction and precipitation, it is important that specimens be analyzed the same day that they are received in the laboratory. If there is to be any delay in analysis, specimens should be acidified with nitric acid and frozen.

Thomas P. Moyer, Ph.D.
2/9/83
Revised 7/17/84
Revised 5/13/85

Appendix 8.1.1/3

DETAILED TRACE METAL LABORATORY METHODS
JAPANESE NIES CERTIFIED REFERENCE MATERIAL

環境庁
国立公害研究所

National Institute for Environmental Studies
Japan Environment Agency

Telephone : 0298-51-5111 Cable KOGAIKENTSUKUBA

Yatabe-machi. Tsukuba. Ibaraki 305 Japan

OCCUPATIONAL HEALTH & SAFETY DIVISION
JUL -5 1985
Laboratory Services Branch

March, 1985

NIES Certified Reference Material, Human Hair

The National Institute for Environmental Studies(NIES) announces the availability of NIES Certified Reference Material No.5, Human Hair.

Trace element analysis of human hair has been carried out in laboratories throughout the world for the purpose of assessing the nutritional and toxicological status of the individual. In order to assist the validation of analytical procedures, a hair reference material certified for elemental composition has been prepared. The material was prepared from human scalp hair (Japanese male, black in colour) collected from barber shops in Tsukuba and Tokyo. The scalp hair was washed in a nonionic detergent solution in an ultrasonic cleaner, dried, ground in an agate ball-mill (planetary type), sieved through a polyethylene net, blended, bottled and finally sterilized by Co-60 radiation. The bottles contain about 2 grams of material.

Certified values are provided for Ca, Cd, Cr, Cu, Fe, Hg, K, Mg, Mn, Na, Ni, Sr and Zn, while reference values are reported for Al, Ba, Br, Cl, Co, P, Pb, Rb, Sb, Sc, Se and Ti. The elemental composition of this reference material is considered similar to "normal values" of the Japanese male population.

For further information on the availability of NIES environmental reference materials, write to Dr. K. Okamoto at the National Institute for Environmental Studies, Yatabe-machi, Tsukuba, Ibaraki, 305 Japan.

Preparation of Material

The scalp hair (about 20 kg) for this reference material was male scalp hair and was collected from three barber shops in Tsukuba and Tokyo. After removal of visible contaminants, the hair was washed by ultrasonic cleaning (20 min) in a 0.3 % nonionic detergent (polyethylene glycol mono-lauryl ether) solution, and then the detergent was removed by copious rinse with distilled water. The cleaned hair was dried in an air-oven at 80 ℃ overnight.

For pulverizing the hair sample, several apparatus were tested from the viewpoints of grinding efficiency and contamination, since hair is a most difficult material to be pulverized. As a result, an agate ball-mill (planetary type) was selected as technically the best method, though contamination with small portion of agate debris was unavoidable. About 60 g of the hair was ground initially in the agate ball-mill (250 ml x 4) and this procedure was repeated for about 2 kg of the cleaned hair. The pulverized powder was sieved through a polyethylene net to remove undestroyed fibrous hair. The sieved powder was mixed in a V-blender (150 L) for 2 hrs and packaged into acid-washed vials (1100 vials, 2 g each). The bottles were sterilized by Co-60 radiation (2 M rad) at the Japan Atomic Energy Research Institute (Takasaki).

Homogeneity Assessment

In order to estimate homogeneity of the material, the variation of elemental content in several bottles was examined by acid-digestion followed by inductively coupled plasma atomic emission spectrometry and atomic absorption spectrometry analysis. Five bottles were randomly selected from the lot of 1,100 bottles and 5 aliquots (about 200 mg dry weight) were taken from each bottle (total 25 samples).

The homogeneity of the hair reference material was estimated using the analysis of variance. For the elements Ca, Fe, Mg, Zn, Na, Cu, Mn and Sr, variations due to sample variability were estimated to be less than 1 % (as relative standard deviation), indicating that the prepared Hair satisfies the homogeneity criteria for a reference material.

Certified Values

The certified values are based on results of determinations by at least three independent analytical techniques. The uncertainties of the certified values were estimated based on consideration of 2 times the standard deviation of the mean of the acceptable values, and of the 95 % confidence intervals for the mean of individual methods.

Sample Size

A minimum sample weight of 200 mg of the dry material should be used. A homogeneity test varying the sample size from 20 mg to 200 mg showed the best homogeneity for the 200 mg sample.

The material readily adheres to the wall of glass and Teflon vessels by electrostatic attraction and care should be taken in transfer operations.

Instruction for Drying

The material should be dried in an air-oven at 85 ℃ for 4 hrs before use. The moisture loss should be determined for each bottle (ranging from 6 % to 9 %). For the determination of volatile elements such as Hg and Se, drying should be done on samples separate to those for analysis.

Storage

The material should be kept tightly closed in its original bottle and stored in a desiccator at room temperature.

Additional Information

This reference material contains debris of an agate ball-mill, namely SiO_2, used for pulverization of the material. The certified and reference values are based on analyses performed on the *entire* sample. Therefore, decomposition procedures should be designed to achieve complete dissolution of the material such as through the use of a mixture of nitric/perchloric/hydrofluoric acids.

It is recommended to remove from the sample being analysed fibrous hair which, occasionally, may be present in the vial.

Analytical Values
NIES Reference Material No.5
"Human HAIR"

Certified Values

Element	Content*(μg/g)
Calcium^{a,c,d,e,f}	728 ± 30
Iron^{a,c,e,f}	225 ± 9
Magnesium^{a,c,e}	208 ± 10
Zinc^{a,c,d,e}	169 ± 10
Potassium^{a,b,c,d,e}	34 ± 3
Sodium^{a,b,c,e}	26 ± 1
Copper^{a,c,d,e}	16.3 ± 1.2
Manganese^{a,c,e}	5.2 ± 0.3
Mercury^{a,e,g,h}	4.4 ± 0.4
Strontium^{c,d,e}	2.3 ± 0.2
Nickel^{a,d,e}	1.8 ± 0.1
Chromium^{a,c,e}	1.4 ± 0.2
Cadmium^{a,d,e}	0.20 ± 0.03

a: atomic absorption spectrometry, b: flame emission spectrometry,
c: inductively coupled plasma emission spectrometry,
d: isotope dilution mass spectrometry, thermal ionization,
e: neutron activation analysis, f: spectrophotometry,
g: atomic fluorescence spectrometry,
h: microwave induced plasma emission spectrometry,

Reference Values

Content*(μg/g)

Chlorine	250	Barium	3.2
Aluminum	240	Selenium	1.4
Phosphorus	165	Rubidium	0.19
Bromine	90	Cobalt	0.10
Titanium	22	Antimony	0.07
Lead	6.0	Scandium	0.05

*Based on dry weight; The material should be dried in an air-oven at 85°C for 4 hrs before use (moisture content 6 % - 9 %). A minimum sample size of 200 mg of the dry material should be used.

Yatabe-machi, Tsukuba,
Ibaraki, 305
March, 1985

National Institute
for Environmental Studies
Environment Agency of Japan

Appendix 9.10

QUALITY CONTROL OF RITUALISTIC MEDICAL EXAMINATIONS

Appendix 9.10

QUALITY CONTROL OF RITUALISTIC MEDICAL EXAMINATIONS

Pre-Test Results

The results of physician examiner rating of twenty-two video-taped physical abnormalities are displayed on Table 9.10. The problems presented included skin rashes, drum abnormalities, neurological abnormalities and masses in a number of anatomical locations. Physician examiners used selected parts of the rating form to rate their interpretation of the physical abnormalities being presented.

More than 80% of the abnormalities presented were detected by physician examiners who initiated their employment with the project in June and August. The detection rate of the July physician group was considered to be less than desirable. As a result additional orientation and review time was added prior to their entry into the data collection process in the field.

Field Data Results

Conventional methods of evaluating inter-observer agreement were not applicable to the ritualistic examination data since variation attributable to differences among examiners is confounded with variation attributable to differences among subjects.

Inter-observer agreement was, therefore, estimated with descriptive analyses using the following assumption and hypotheses:

Assumption 1	The distribution of subjects among examiners in the five age categories (0-1, 2-5, 6-9, 10-18, 18+) is homogeneous and, therefore, the proportionate number of abnormalities identified should be equivalent.
Hypothesis 1A	There will be no difference in the overall proportion of abnormalities detected among physician examiners examining more than 10% of subjects in each of the study areas and age groups.

1B There will be no difference in the proportion of abnormal cardinal signs detected among physicians examining more than 10% of subjects in each of the study areas and age groups.

Note: The pragmatics of the field operation did not permit subjects to be randomly allocated to physician examiners. There was a systematic effort made to have physicians with training in pediatrics examine the younger age groups (0-1, 2-5, 6-9) hence the descriptive analysis summarizes proportionate detection rates in each age group separately. Apart from these considerations examiners evaluated subjects on a first come, first serve basis.

Cardinal signs were items included as a nominal dependent variables in the comparative analysis of health status across areas. As estimation, therefore, of inter-observer agreement on these items was included as a separate and important aspect of the analysis.

Results

Table 9.11 provides a demographic summary of the number of subjects within age groups and areas studied along with the number of physician examiners in each age and study area grouping. The number of physicians examining more than 10% of subjects has also been indicated. Variation in the proportion of physicians examining more than 10% of subjects is within range of 25 to 100 percent. This is attributed to differences in the size of the sample in each age group and study area as well as the varying length of employment of physician examiners on the project (one to three months). Since physicians examining more than 10% of the subject population could be expected to contribute a greater portion of the potential observer bias, they have been identified in most instances as a subpopulation in the analysis.

Table 9.12 summarizes the overall proportionate percent of signs detected by physician examiners in each age group. The proportion of detected abnormalities was low in all age groups. The range of detection rates among examiners was minimal in the 6-9 year age groups (0.81%). The greatest difference in detection rates were in the 2-5 year age group (3.23%). Generally the detection rates among examiners were reasonably consistent over all items evaluated for each age group. Substantial differences in detection rates could exist on individual items of the examination even though overall detection rates were similar. If particular concern were differences in detection which may exist in the evaluation of those cardinal signs which were employed as dependent variables in the comparative analysis across study groups.

Table 9.13/1 to 9.13/5 provide a breakdown of proportionate abnormal sign detection rates among all examiners gathering data in each age group and study area. The number of subjects by area, age group and examiner has been indicated along with those examiners who collected data on more than 10% of subjects.

Although detection rates in the 0-1 age group would appear to be equivalent across examiners and areas, the number of subjects available for examination in this age group limits the ability to describe any trends in examiner behavior.

In the remaining age groups, equivalence of detection rates were not substantiated particularly in the first two cardinal signs; red eyes and red mucosa. Variation in detection rates is still present in the subsample of examiners who saw more than 10% of subjects even when their subject pools were more or less equivalent in size. This may be attributable to differences in the subjects examined by different physicians. However, if one assumes the worst possibility, that being the variation in detection rates is primarily attributable to difference among examiners, then one would want to be assured that those differences persisted across the study areas being compared.

Table 9.14/1 and 9.14/2 provide a summary of the range of detection rates across areas in each age group. The interval between the examiner detecting the fewest number of abnormal findings to the examiner detecting the greatest number of finding is provided in the form of a percentage difference. Again it can be noted that differences in the range of detect abnormalities differ across study areas with the two cardinal signs red eyes and red mucosa along with peripheral nerve abnormalities in the 18+ age group and drum abnormalities in the 10-18 year age group. It should be noted, however, that the range of abnormality detection across areas for any one examiner differs by about the same interval. This would suggest that differences in range of detection rates across the study areas were more likely affected by differences in the subjects being examined and their distribution among examiners or inconsistency within the examiners themselves throughout the three months of data collection.

The results of standardized patient analysis provide important supplementary information in this study about the potential contribution of examiner bias to variation in cardinal signs observed within and across study areas.

Standardized Patient Results

Standardized patients provided a method of examining observer variation unconfounded by differences in subjects, location, time; analogous to the concept of standardized lab samples, standardized patients were sent through one examination team periodically, their status being unknown to the examiners on site. The purpose of doing so was to estimate the contribution of observer variation to the variation in the populations being studied. Table 9.15 provides a summary of examiner agreement for each item included in the cardinal signs employed in data analysis. It can be noted that agreement among examiners was generally exceptionally good. When this is compared with Koran's (1975) summary of reported rates of physician agreement on physical signs, the examiners' studied were consistently above reported percent agreements in most signs (range of reported agreement = 54-100%). The poorest level of agreement is present on the rating of the sclera in the composite variable red eye; the rating of a variety of drum abnormalities and intention tremor. Differences in observer rating could explain a portion of the variation in detection rates noted with red eyes and drum abnormalities. The standardized patient data would not suggest however that observer variation contributed in any major way to the variation observed in the study data.

REFERENCE

Koran L M. The reliability of clinical methods, data and judgements. New Engl J Med September 1975;293(3).

TABLE 9.10

RITUALISTIC EXAMINATION PRE-TEST RESULTS: % ABNORMAL FINDINGS DETECTED

	June	July	August
N	4	7	3
Abnormal Items			
% Abnormal Items Detected	90.1	77.8	81.6

TABLE 9.11

Ritualistic Exam: Number of Subjects (Ss) and Physician Examiners Within Age Groups By Study Area

~~Area~~		Age Group					
Area		0-1	2-5	6-9	10-18	18+	Total.
1.A.	No. ND.	4	14	17	17	18	
	No examining >10% of Subjects	3	3	2	4	5	
	No S.S.	38	216	219	415	1263	2151
2.R.	No MD	2	11	13	13	15	
	No examining >10% subjects	2	5	5	4	4	
	No. SS	4	113	92	184	423	816
CCI	No HD	1	9	10	11	12	
	No examining >10% subjects	1	2	5	6	8	
	No SS	2	103	69	114	328.	616
Total		44	465	437	826	2265	3583

Table 9.12. Ritualistic Examination. Overall % Proportion of Signs Detected, Not Detected Across Examiners by Age Group.

EXAMINER.	AGE GROUP 0 - 1YRS %Signs Present	%Signs Absent	2 - 5 YRS %Signs Present	% Signs Absent	6 - 9 YRS %Signs Present	% Signs Absent	10 - 18 YRS %Signs Present	% Signs Absent	18+ YEARS % Signs Present	% Signs Absent
MD^a 2	2.44	97.56	0.42	99.58	0.27	99.73	0.27	99.73	1.45	98.55
3	4.61	95.39	1.08	98.92	0.83	99.17	1.12	98.88	1.84	98.16
4			1.52	98.48	0.80	99.20	1.32	98.68	2.28	97.72
5			0.81	99.19	0.98	99.02	0.94	99.06	1.56	98.44
6	2.58	97.42	0.53	99.47	0.83	99.17	0.67	99.33	1.53	98.47
7			0.26	99.74	0.56	99.44	0.90	99.10	1.79	98.21
8	3.14	96.86	0.65	99.35	0.99	99.01	0.96	99.04	2.56	97.44
9			3.44	96.56	1.81	98.19	1.66	98.34	1.50	98.50
11	3.14	96.86	0.65	99.35	0.47	99.53	0.51	99.49	1.53	98.47
12	2.73	97.27	0.35	99.65	0.34	99.66	0.65	99.35	1.08	98.92
13	1.85	98.15	0.18	99.82	0.55	99.45	0.45	99.55	1.32	98.68
14			0.44	99.56	0.61	99.39	0.60	99.40	1.54	98.46
15			0.59	99.41	0.40	99.60	0.86	99.14	1.60	98.40
16			0.39	99.61	0.43	99.57	0.74	99.26	1.60	98.40
17			0.70	99.30	0.60	99.40	0.86	99.14	1.51	98.49
18			0.08	99.92	0.41	99.52	0.64	99.36	1.15	98.85
25	2.58	97.42	0.21	99.79	0.18	99.82	0.35	99.65	0.70	99.30
72					0.26	99.74				
99	2.58	97.42	0.78	99.22	0.77	99.23	0.08	99.92	1.41	98.59
% difference in range.	2.76%		3.23%		0.81%		1.66%		1.80%	

TABLE 9.13/1

PERCENTAGE PROPORTION ABNORMAL CARDINAL SIGNS SELECTED BY PHYSICIAN EXAMINERS IN AGE GROUP 0-1 (N = 44) ACROSS STUDY AREAS

AREA

CARDINAL SIGNS	IA (Ss = 38)									SR (Ss = 4)									DCCI (Ss = 2)								
MD#	2	3	6	8	11	12	13	25	99	2	3	6	8	11	12	13	25	99	2	3	6	8	11	12	13	25	99
No Ss per exam.	(10)	(2)*	(1)*	(0)	(4)	(17)	(1)*	(2)*	(1)*	(0)	(0)	[illegible]	(2)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)
1) Red eyes.	0	0	0	NA	0	0	0	0	0	NA	NA	NA	0	0	NA	NA	N/A	N/A	N/A	NA	NA	N/A	N/A	N/A	N/A	0	N/A
2) Red mucosa	0	0	0	NA	25.	0	0	0	0	N/A	N/A	N/A	0	0	N/A	N/A	NA	NA	N/A	NA	NA	N/A	NA	N/A	N/A	0	N/A
3) Drum Abn.	0	0	0	N/A	0	0	0	0	0	N/A	N/A	N/A	0	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	0	N/A
4) Lung Wheezes/Crackles	0	0	0	N/A	0	0	0	0	0	N/A	N/A	NA	0	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	0	NA
5) Periph. Nerve Involvement	0	0	0	N/A	0	0	0	0	0	N/A	N/A	0	0	0	N/A	NA	NA	NA	N/A	NA	N/A	NA	NA	N/A	N/A	0	N/A
6) Tremor	0	0	0	N/A	0	0	0	0	0	N/A	NA	0	0	0	N/A	NA	NA	N/A	N/A	N/A	NA	NA	NA	NA	NA	0	N/A
7) Skin Lesion.	0	0	0	N/A	0	0	0	0	0	NA	NA	0	0	0	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	0	N/A

NA : Examiner did not examine any subject

* : Examiner examined <10% of Subjects

TABLE 9.13/2

PERCENTAGE PROPORTION ABNORMAL CARDINAL SIGNS
DETECTED BY PHYSICIAN EXAMINERS
IN AGE GROUP 2-5 (N = 465) ACROSS STUDY AREAS

AREA

IA (Ss = 216)

CARDINAL SIGNS MD#	2	3	4	5	6	7	8	9	11	12	13	14	15	16	17	18	25	99
(Nss per exam)	(35)	(14)*	(6)*	(15)*	(12)*	(9)*	(4)*	(3)*	(22)	(74)	(2)*	(8)*	(0)*	(0)*	(0)*	(0)*	(2)*	(5)*
1) Red eyes)	0	0	0	0	0	0	0	0	0	1.4	0	0	NA	NA	NA	NA	50.0	0
2) Red mucosa	0	14.3	50.0	0	8.3	11.1	0	33.3	13.6	0	0	12.5	NA	NA	NA	NA	50.0	20.0
3) Drum Abnorm.	0	0	0	0	0	0	0	0	0	0	0	0	NA	NA	NA	NA	0	0
4) Lung Wheeze/Crackle	0	0	0	0	0	0	0	0	0	0	0	0	NA	NA	NA	NA	0	0
5) Periph Nerv. Involv.	0	0	0	0	0	0	0	0	0	0	0	0	NA	NA	NA	NA	0	0
6) Tremor	0	0	0	0	0	0	0.	0	0	0	0	0	NA	NA	NA	NA	0	0
7) Skin Lesion.	2.9	0	0	0	0	0	0	0	4.6	1.4	0	0	NA	NA	NA	NA	0	0

SR (Ss = 113)

CARDINAL SIGNS MD#	2	3	4	5	6	7	8	9	11	12	13	14	15	16	17	18	25	99
(Nss per exam)	(0)*	(15)	(12)	(0)*	(2)*	(0)*	(2)*	(8)*	(20)	(17)	(0)*	(0)*	(5)*	(2)*	(1)*	(0)*	(29)	(0)*
1) Red eyes)	NA	0	50.	NA	0	NA	0	0	0	23.5	NA	NA	0	0	0	NA	6.9	NA
2) Red mucosa	NA	53.3	75.0	NA	0	NA	0	12.5	15.0	5.8	NA	NA	20.0	0	0	NA	3.5	NA
3) Drum Abnorm.	NA	0	0	NA	0	NA	0	0	0	0	NA	NA	0	0	0	NA	0	NA
4) Lung Wheeze/Crackle	NA	0	0	NA	0	NA	0	0	0	0	NA	NA	0	0	0	NA	0	NA
5) Periph Nerv. Involv.	NA	0	0	NA	0	NA	0	0	0	0	NA	NA	0	0	0	NA	0	NA
6) Tremor	NA	0	0	NA	0	NA	0	0	0	0	NA	NA	0	0	0	NA	0	NA
7) Skin Lesion.	NA	0	0	NA	0	NA	0	0	5.0	0	NA	NA	0	0	0	NA	0	NA

DCCI (Ss = 103)

CARDINAL SIGNS MD#	2	3	4	5	6	7	8	9	11	12	13	14	15	16	17	18	25	99
(Nss per exam)	(0)*	(9)*	(1)*	(0)*	(0)*	(0)*	(1)*	(0)*	(0)*	(39)	(9)*	(0)*	(5)*	(0)*	(4)*	(5)*	(30)	(0)*
1) Red eyes)	NA	0	100.	NA	NA	NA	0	NA	NA	5.1	0	NA	0	NA	0	0	0	NA
2) Red mucosa	NA	0	0	NA	NA	NA	0	NA	NA	2.6	0	NA	20.0	NA	0	0	0	NA
3) Drum Abnorm.	NA	0	0	NA	NA	NA	0	NA	NA	0	0	NA	0	NA	0	0	0	NA
4) Lung Wheeze/Crackle	NA	0	0	NA	NA	NA	0	NA	NA	0	0	NA	0	NA	0	0	0	NA
5) Periph Nerv. Involv.	NA	0	0	NA	NA	NA	0	NA	NA	0	0	NA	0	NA	0	0	0	NA
6) Tremor	NA	0	0	NA	NA	NA	0	NA	NA	0	0	NA	0	NA	0	0	0	NA
7) Skin Lesion.	NA	0	0	NA	NA	NA	0	NA	NA	0	0	NA	0	NA	0	0	0	NA

NA : Examiner did not examine any subjects
* : Examiner examined < 10% of subjects

TABLE 9.13/3

RITUALISTIC EXAMINATION: PERCENTAGE PROPORTION ABNORMAL CARDINAL SIGNS DETECTED BY PHYSICIAN EXAMINER IN AGE GROUP 6-9 (N = 437) ACROSS STUDY AREAS

AREA

IA (Ss = 219)

CARDINAL SIGNS MD*	2	3	4	5	6	7	8	9	11	12	13	14	15	16	17	18	25	72	99
No. Ss/examiner	(20)	(25)	(19)	(6)	(13)	(15)	(16)	(3)	(13)	(54)	(13)	(15)	(1)	(0)	(1)	(6)	(1)	(1)	(3)
1) Red eyes.	0	0	6.3	0	7.7	0	0	0	0	1.9	0	0	0	NA	0	NA	0	0	0
2) Red mucosa	5.0	20.0	36.8	16.7	15.4	0	0	0	0	1.9	0	13.3	0	NA	100.	NA	0	0	66.7
3) Drum Abnorm.	0	0	0	0	0	0	0	0	0	0	0	0	0	NA	0	NA	0	0	0
4) Lung Wheeze/Crackle	0	0	0	0	0	0	0	0	0	0	0	0	0	NA	0	NA	0	0	0
5) Periph Nerve Involvement	0	4.0	0	16.7	0	6.7	6.3	0	0	0	7.7	0	0	NA	0	NA	0	0	0
6) Tremor	0	0	0	0	0	0	0	0	0	0	0	0	0	NA	0	NA	0	0	0
7) Skin Lesion	0	0	0	0	7.7	6.7	13.5	0	0	1.9	7.7	0	0	NA	0	NA	0	0	0

SR (Ss = 92)

CARDINAL SIGNS MD*	2	3	4	5	6	7	8	9	11	12	13	14	15	16	17	18	25	72	99
No. Ss/examiner	(0)	(11)	(12)	(6)	(3)	(0)	(6)	(6)	(10)	(7)	(4)	(0)	(9)	(3)	(2)	(1)	(18)	(0)	(0)
1) Red eyes.	NA	0	8.3	NA	0	NA	0	0	0	57.1	0	NA	0	0	0	0	11.1	NA	NA
2) Red mucosa	NA	36.4	83.3	NA	0	NA	0	0	0	0	0	NA	0	0	0	0	5.6	NA	NA
3) Drum Abnorm.	NA	0	0	NA	0	NA	0	0	0	0	0	NA	0	0	0	0	0	NA	NA
4) Lung Wheeze/Crackle	NA	0	0	NA	0	NA	0	0	0	0	0	NA	0	0	0	0	0	NA	NA
5) Periph Nerve Involvement	NA	0	0	NA	0	NA	16.7	0	0	0	0	NA	11.1	0	0	0	0	NA	NA
6) Tremor	NA	0	0	NA	0	NA	0	0	0	0	0	NA	0	0	0	0	0	NA	NA
7) Skin Lesion	NA	0	8.3	NA	33.3	NA	0	0	0	0	0	NA	0	0	0	0	0	NA	NA

DCCI (Ss = 69)

CARDINAL SIGNS MD*	2	3	4	5	6	7	8	9	11	12	13	14	15	16	17	18	25	72	99
No. Ss/examiner	(0)	(3)	(5)	(0)	(1)	(0)	(7)	(0)	(0)	(22)	(4)	(0)	(8)	(0)	(6)	(4)	(11)	(0)	(0)
1) Red eyes.	NA	0	0	NA	0	NA	0	NA	NA	4.6	0	NA	0	NA	0	0	0	NA	NA
2) Red mucosa	NA	0	66.7	NA	0	NA	0	NA	NA	0	0	NA	0	NA	16.7	36.4	0	NA	NA
3) Drum Abnorm.	NA	0	0	NA	0	NA	0	NA	NA	0	0	NA	0	NA	0	0	0	NA	NA
4) Lung Wheeze/Crackle	NA	0	0	NA	0	NA	0	NA	NA	0	0	NA	0	NA	0	0	0	NA	NA
5) Periph Nerve Involvement	NA	0	0	NA	0	NA	0	NA	NA	4.5	0	NA	0	NA	0	0	0	NA	NA
6) Tremor	NA	0	0	NA	0	NA	0	NA	NA	0	0	NA	0	NA	0	0	0	NA	NA
7) Skin Lesion	NA	0	0	NA	0	NA	0	NA	NA	0	0	NA	0	NA	0	0	0	NA	NA

NA: Examiner did not examine any subjects

*: Examiner examined < 10% of subjects

TABLE 9.13/4

RITUALISTIC EXAMINATION: PERCENTAGE PROPORTION ABNORMAL CARDINAL SIGNS DETECTED BY PHYSICIAN EXAMINERS IN AGE GROUP 10-18 (N = 826) ACROSS STUDY AREAS

AREA

IA (Ss = 415)

CARDINAL SIGNS	2	3	4	5	6	7	8	9	11	12	13	14	15	16	17	18	25	99
MD#	2	3	4	5	6	7	8	9	11	12	13	14	15	16	17	18	25	99
(Nos/examiner)	(11)*	(49)	(50)	(13)*	(39)*	(15)*	(50)	(16)*	(26)*	(72)	(17)*	(31)*	(8)*	(4)*	(6)*	(0)*	(4)*	(4)*
1) Red eyes	0	4.1	14.0	0	7.7	6.7	18.0	0	3.9	12.5	0	3.2	0	0	0	NA	0	0
2) Red mucosa	0	20.4	54.0	7.7	15.4	6.7	6.0	6.3	7.7	9.7	5.9	0	0	50.0	16.7	NA	0	0
3) Drum Abnorm	0	4.1	14.0	0	0	20.0	0	0	0	0	0	0	12.5	0	33.3	NA	0	0
4) Lung wheeze/Crackle	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	NA	0	0
5) Peripheral Nerve Involve.	0	0	2.0	7.7	2.6	0	4.0	0	0	0	0	3.2	12.5	0	0	NA	0	0
6) Tremor	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	NA	0	0
7) Skin Lesion	0	16.3	2.0	0	0	6.7	12.0	0	3.9	2.8	0	0	0	0	0	NA	0	0

SR (Ss = 184)

CARDINAL SIGNS	2	3	4	5	6	7	8	9	11	12	13	14	15	16	17	18	25	99
MD#	2	3	4	5	6	7	8	9	11	12	13	14	15	16	17	18	25	99
(Nos/examiner)	(0)*	(35)	(15)*	(0)*	(4)*	(0)*	(17)*	(7)*	(18)	(15)*	(18)	(0)*	(16)*	(5)*	(8)*	(8)*	(18)	(0)*
1) Red eyes	NA	0	26.7	NA	0	NA	35.3	0	5.6	46.7	5.6	NA	6.3	0	0	0	27.8	NA
2) Red mucosa	NA	57.2	93.3	NA	25.0	NA	0	28.6	5.6	6.7	0	NA	6.3	0	50.0	0	0	NA
3) Drum Abnorm	NA	8.6	6.7	NA	0	NA	0	0	0	0	0	NA	6.3	0	0	0	0	NA
4) Lung wheeze/Crackle	NA	2.9	0	NA	0	NA	0	0	0	0	0	NA	0	0	0	0	0	NA
5) Peripheral Nerve Involve.	NA	2.9	0	NA	0	NA	0	0	0	0	5.6	NA	12.5	0	0	0	0	NA
6) Tremor	NA	0	0	NA	0	NA	0	0	0	0	0	NA	0	0	0	0	0	NA
7) Skin Lesion	NA	5.7	0	NA	0	NA	0	0	0	13.3	11.1	NA	0	0	0	0	0	NA

DCCI (Ss = 114)

CARDINAL SIGNS	2	3	4	5	6	7	8	9	11	12	13	14	15	16	17	18	25	99
MD#	2	3	4	5	6	7	8	9	11	12	13	14	15	16	17	18	25	99
(Nos/examiner)	(0)*	(8)*	(16)	(0)*	(0)*	(0)*	(14)	(0)*	(0)*	(13)	(10)*	(2)*	(6)*	(11)	(8)*	(15)	(11)	(1)*
1) Red eyes	NA	0	25.0	NA	NA	NA	0	NA	NA	30.8	0	0	0	0	0	0	0	0
2) Red mucosa	NA	25.0	43.8	NA	NA	NA	7.1	NA	NA	15.4	0	50.0	0	18.2	37.5	13.3	0	0
3) Drum Abnorm	NA	12.5	31.3	NA	NA	NA	0	NA	NA	0	0	0	0	0	0	6.7	0	0
4) Lung wheeze/Crackle	NA	0	6.3	NA	NA	NA	0	NA	NA	0	0	0	0	0	0	0	0	0
5) Peripheral Nerve Involve.	NA	12.5	0	NA	NA	NA	0	NA	NA	0	0	0	33.3	9.1	0	0	0	100
6) Tremor	NA	0	0	NA	NA	NA	0	NA	NA	0	0	0	0	0	0	0	0	0
7) Skin Lesion	NA	25.0	0	NA	NA	NA	0	NA	NA	0	0	0	0	0	12.5	6.7	0	0

NA. Examiners did not examine any subjects

* : Examiners examined <10% of subjects

TABLE 9.13/5

RITUALISTIC EXAMINATION: PERCENTAGE PROPORTION OF ABNORMAL CARDINAL SIGNS DETECTED BY PHYSICIAN EXAMINERS IN AGE GROUP 18+ (N = 2265) ACROSS STUDY AREAS

AREA

IA (Ss = 1263)

CARDINAL SIGNS MD‡	2	3	4	5	6	7	8	9	11	12	13	14	15	16	17	18	25	99
(Nos./examiner)	(40)*	(152)	(193)	(64)*	(125)	(106)*	(151)	(50)*	(28)*	(22)*	(127)	(101)*	(27)*	(27)*	(24)*	(1)*	(7)*	(18)*
1) Red mucosa	3.0	14.5	33.1	7.8	19.2	7.6	11.9	4.0	3.6	9.1	1.6	6.0	0	18.5	45.8	0	0	22.2
2) Drum Abnorm	2.5	17.8	36.3	9.4	13.6	21.7	5.3	4.0	14.3	0	3.9	6.9	7.4	11.1	37.5	0	0	5.6
3) Lung wheezes	5.0	5.9	6.2	1.6	2.4	4.7	3.3	4.0	0	0	2.4	5.9	14.8	7.4	4.2	0	0	5.6
4) Red eyes	0	4.0	16.1	9.4	18.4	5.7	54.6	4.0	9.6	27.3	4.7	2.0	3.7	18.5	12.5	0	28.6	5.6
5) Periph. Nerve Involvement	22.5	23.1	16.7	12.5	13.6	17.0	19.2	30.0	10.7	4.6	24.4	21.5	37.0	14.8	8.3	0	0	38.9
6) Tremor	2.5	0.7	0	1.6	0.8	2.8	1.3	0	0	0	0	1.0	0	7.4	0	0	0	0
7) Skin Lesion	0	5.4	5.7	9.4	0	7.5	9.3	0	10.7	0	2.4	0	0	0	0	0	0	0

SR (Ss = 423)

CARDINAL SIGNS MD#	2	3	4	5	6	7	8	9	11	12	13	14	15	16	17	18	25	99
(Nos./examiner)	(0)*	(64)	(55)	(0)*	(19)*	(1)*	(54)	(35)*	(17)*	(9)*	(41)*	(3)*	(43)	(23)*	(23)*	(12)*	(19)*	(0)*
1) Red mucosa	NA	57.8	38.2	NA	5.3	0	9.3	11.4	41.2	22.2	2.4	0	9.3	8.7	47.8	0	0	NA
2) Drum Abnorm	NA	15.6	34.6	NA	5.3	0	5.6	5.7	0	0	4.9	0	9.3	21.7	21.7	33.3	0	NA
3) Lung wheezes	NA	7.3	10.9	NA	0	0	1.9	5.7	0	0	0	0	4.7	0	8.7	0	10.5	NA
4) Red eyes	NA	7.3	58.2	NA	15.8	0	68.5	17.1	11.8	44.4	2.4	0	4.7	17.4	17.4	0	21.1	NA
5) Periph. Nerve Involvement	NA	14.6	5.5	NA	5.3	0	9.3	14.3	17.7	22.2	9.8	66.7	32.6	21.8	0	0	0	NA
6) Tremor	NA	0	0	NA	0	0	0	0	0	0	0	0	0	0	0	0	0	NA
7) Skin Lesion	NA	4.4	3.6	NA	0	0	0	0	0	0	2.4	0	0	8.7	8.7	0	0	NA

DCCI (Ss = 328)

CARDINAL SIGNS MD‡	2	3	4	5	6	7	8	9	11	12	13	14	15	16	17	18	25	99
(Nos./examiner)	(0)*	(43)	(34)	(0)*	(2)*	(0)*	(46)	(0)*	(0)*	(0)*	(38)	(1)*	(36)	(42)	(39)	(32)	(14)*	(1)*
1) Red mucosa	NA	23.3	55.9	NA	0	NA	0	NA	NA	NA	0	100	0	0	15.4	6.3	0	0
2) Drum Abnorm	NA	16.3	50.0	NA	0	NA	4.4	NA	NA	NA	0	0	8.3	14.3	12.8	6.3	0	0
3) Lung wheezes	NA	4.7	8.8	NA	0	NA	0	NA	NA	NA	0	0	2.8	0	7.7	0	7.1	0
4) Red eyes	NA	4.7	26.5	NA	0	NA	6.5	NA	NA	NA	5.3	0	2.8	9.5	10.3	0	0	0
5) Periph. Nerve Involvement	NA	16.3	5.9	NA	0	NA	10.9	NA	NA	NA	15.8	NA	30.6	4.8	7.7	12.5	0	0
6) Tremor	NA	0	0	NA	0	NA	0	NA	NA	NA	0	0	0	7.1	0	3.1	0	0
7) Skin Lesion	NA	2.3	5.9	NA	0	NA	2.2	NA	NA	NA	2.6	0	0	9.5	0	0	0	0

NA: Examiner did not examine any subjects

* Examiner examined < 10% of subjects.

TABLE 9.14/1

THE PERCENTAGE INTERVAL BETWEEN THE EXAMINER DETECTING THE LOWEST PERCENT OF CARDINAL FINDINGS AND HIGHEST PERCENT OF CARDINAL FINDINGS IN EACH STUDY AREA BY AGE GROUP

Cardinal Signs	Age Groups														
	0-1 years			2-5 years			6-9 years			10-18 years			18+ years		
	IA	SR	DCCI	IA	SR	DCCI	IA	SR	DCCI	IA	SR	DCCI	IA	SR	DCCI
(No. Examiners)	(4)	(2)	(1)	(14)	(11)	(9)	(17)	(13)	(10)	(17)	(13)	(11)	(18)	(15)	(12)
1) Red eyes	0.0	0.0	0.0	50.0	50.0	100.0 **	7.7	57.1	4.6 **	18.0	35.3	30.8 *	59.6	68.5	28.5 **
2) Red Mucosa	25.0	0.0	0.0	50.0	75.0	20.0 **	66.7	83.3	66.7 *	54.0	93.3	37.5 **	46.8	78.2	55.9 **
3) Drum Abnorm	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	33.3	8.6	31.3 **	36.3	34.6	50.0 *
4) Lung Wheezes/Crackles	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	2.9	6.3	14.8	10.9	8.8
5) Unilateral Nerve Involve.	0.0	0.0	0.0	0.0	0.0	0.0	16.7	16.7	4.6 *	12.5	12.5	33.3 **	38.9	66.7	30.6 **
6) Tremor	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	7.4	0.0	7.1
7) Skin Lesion	0.0	0.0	0.0	4.6	5.0	0.0	12.5	33.3	0.0 **	16.3	13.3	25.0 *	10.7	8.7	9.5

* % range interval of proportionate detection rates differed among study areas by 10-20%

** % range interval of proportionate detection rates differed among study areas by >20%

TABLE 9.14/2

RITUALISTIC EXAMINATION: PERCENTAGE INTERVAL BETWEEN THE EXAMINER DETECTING THE LOWEST IN EACH STUDY AREA BY AGE GROUP FOR EXAMINER EXAMINING MORE THAN 10% OF AGE GROUPS BY STUDY AREA. SUBJECTS IN EACH AREA AND AGE GROUP.

CARDINAL SIGNS	0-1 years			2-5 years			6-9 years			10-18 years			18+ years		
	1.A	SR	DocI	IA	SR	Dec I	IA	SR	Dec I	IA	SR	DecI	IA	SR	DecI
No. examiners c >10% subjects	3	2	1	3	4	2	2	5	5	4	4	6	4	4	8
1) Red eyes	0%	0%	0%	1.4%	23.5%	5.1%**	1.9%	11.1%	4.5%*	13.9%	27.8%	25%*	55.7%	63.8%	43.5%**
2) Red mucosa	25%	0%	0%**	13.6%	63.3%	2.5%**	18.3%	83.3%	16.6%**	46%	57.1%	43.8%*	32.1%	68.9%	55.9%**
3) Drum Abnormalities	0%	0%	0%	0%	0%	0%	0%	0%	0%	14.0%	8.6%	31.3%**	32.4%	25.2%	50.0%*
4) Lung wheezes/ Crackles	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	2.9%	6.3%	2.9%	4.0%	8.8%
5) Peripheral Nerve Involvement	0%	0%	0%	0%	0%	0%	4.0%	11.1%	4.5%	4.0%	5.6%	9.1%	5.7%	27.1%	11.5%**
6) Tremor	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	1.3%	0%	7.1%
7) Skin Lesion	0%	0%	0%	3.1%	5.0%	0%	1.4%	8.3%	0%	13.5%	11.1%	6.7%	6.9%	4.3%	4.5%

* % range interval of proportionate detection rates differed among study areas by 10-19%

** % range interval proportionate detection rates differed among study areas by ≥ 20%

TABLE 9.15

RITUALISTIC EXAMINATION: PERCENTAGE INTER-RATER AGREEMENT AMONG PHYSICIAN EXAMINERS WITH STANDARDIZED ADULT PATIENTS BY CARDINAL SIGN

Cardinal Sign	Pt. #1	Pt#2	Pt#3	Pt#4	Pt#5	Pt#6	Average % Agreement By Cardinal Sign
(No. Examiners/Pt)	(3)	(5)	(5)	(2)	(6)	(4)	
RED EYE							
· LID	100.0	100.0	100.0	100.0	100.0	100.0	100.0
· SCLERA	66.7	80.0	100.0	100.0	83.3	75.0	84.2
· CONJUNCT.	100.0	100.0	100.0	100.0	100.0	100.0	100.0
RED MUCOSA							
· NARES	100.0	100.0	100.0	100.0	83.3	100.0	97.2
· BUCCAL	100.0	100.0	100.0	100.0	100.0	100.0	100.0
· PHARYNX	100.0	100.0	100.0	100.0	100.0	100.0	100.0
DRUM ABNORM.	100.0	100.0	100.0	100.0	100.0	100.0	100.0
· INFLAMMATION	100.0	100.0	100.0	100.0	100.0	100.0	100.0
BULGING	100.0	100.0	80.0	100.0	100.0	100.0	96.7
· RETRACTION	100.0	100.0	80.0	100.0	100.0	100.0	96.7
· FLUID	66.7	80.0	80.0	100.0	100.0	75.0	85.6
· PERFORATION	66.7	80.0	80.0	100.0	100.0	100.0	87.8
· SCARRING	100.0	100.0	100.0	100.0	100.0	100.0	100.0
· PE TUBES	100.0	100.0	100.0	100.0	100.0	100.0	100.0
LUNG							
· CRACKLES	100.0	80.0	100.0	100.0	83.3	100.0	93.9
· WHEEZES	100.0	80.0	100.0	100.0	100.0	100.0	96.7
PERIPHERAL NERVE							
· DORSIFLEXOR	100.0	100.0	100.0	100.0	100.0	100.0	100.0
· VIBRATION	100.0	100.0	100.0	100.0	100.0	100.0	100.0
· POSITION	100.0	100.0	100.0	100.0	100.0	100.0	100.0
· ANKLE JERK	100.0	100.0	100.0	100.0	100.0	100.0	100.0
· PIN-FEET	100.0	100.0	80.0	100.0	100.0	100.0	96.7
· PIN-CALF	100.0	80.0	100.0	100.0	100.0	100.0	96.7
TREMOR	100.0	100.0	100.0	100.0	100.0	100.0	100.0
INTENT. TREMOR	100.0	100.0	80.0	50.0	66.6	100.0	82.8
SKIN LESION	100.0	100.0	100.0	100.0	100.0	100.0	100.0
Average Total % Agreement/Case	96.0	95.2	95.2	98.0	96.7	98.0	96.5

Appendix 14.1

CLINICAL DECISIONS AND FOLLOW-UP REGARDING BIOCHEMICAL AND TRACE METAL ABNORMALITIES DETECTED BY THE HEALTH STATUS EVALUATION

Appendix 14.1

CLINICAL DECISIONS AND FOLLOW-UP REGARDING BIOCHEMICAL AND TRACE METAL ABNORMALITIES DETECTED BY THE HEALTH STATUS EVALUATION

I. Biochemical Abnormalities

Among the first 225 serum samples collected during the study there was approximately one biochemical abnormality per sample on average for the following reasons:

1) Abnormality in a biological measurement is often defined arbitrarily as the 5% of values lying outside 2 standard deviations of the mean value. In the current study, 12 different tests were done resulting in a much greater percentage of participants with abnormalities (the exact percentage depending on the relative independence of each biochemical test result).

2) Participants were not asked to come fasting which tended to increase the number of apparent abnormalities in serum calcium, inorganic phosphate and cholesterol.

3) Alkaline phosphatase can be extremely high in children during a growth phase, up to five times the normal adult

range. This made accurate limits difficult to determine for growing children.

4) Strenuous exercise, bruises and other musculoskeletal injuries, which might be especially common among farmers in the study group, can markedly increase serum creatinine kinase.

To reduce the false positive rate and yet not miss important biochemical abnormalities, higher threshold levels were set at which certain tests were termed abnormal. These levels were set with the assistance of Dr. J. K. Todd, Clinical Biochemist and Dr. David Hanley, Endocrinologist, both at the Foothills Hospital in Calgary. Threshold levels were set as follows; serum calcium greater than 2.62 millimoles per litre, serum cholesterol greater than 9.86 millimoles per litre, urate greater than 600 micromoles per litre, urea greater than 10.6 millimoles per litre, bilirubin greater that 24 micromoles per litre, alkaline phosphatase greater than 500 units per litre in those less than 21 years of age and alkaline phosphatase greater than 140 in those at least 21 years of age, lactate dehydrogenase greater than 235 units per litre, aspartate aminotransferase greater than 51 units per litre, and those with a combination of bilirubin, alkaline phosphatase and lactate dehydrogenase each above the Foothills Hospital's clinical laboratory range.

Participants with values outside the normal range either had their blood test repeated in a fasting state, were directly referred to a specialist, or were sent letters with the abnormal biochemical value and a request to have this assessed by their personal physician.

II. Trace Metal Abnormalities

Hair trace metal levels may be difficult to interpret because:

1) The false positive rate for hair is high because hair is easily contaminated by external sources;

2) Whole blood seleniums are approximately 15% to 20% higher than serum selenium samples;

3) Cracked tubes may contaminate the contained blood with cadmium;

4) Hair arsenic abnormalities are best verified by obtaining a urine arsenic level and hair selenium abnormalities are best verified by a serum or plasma sample.

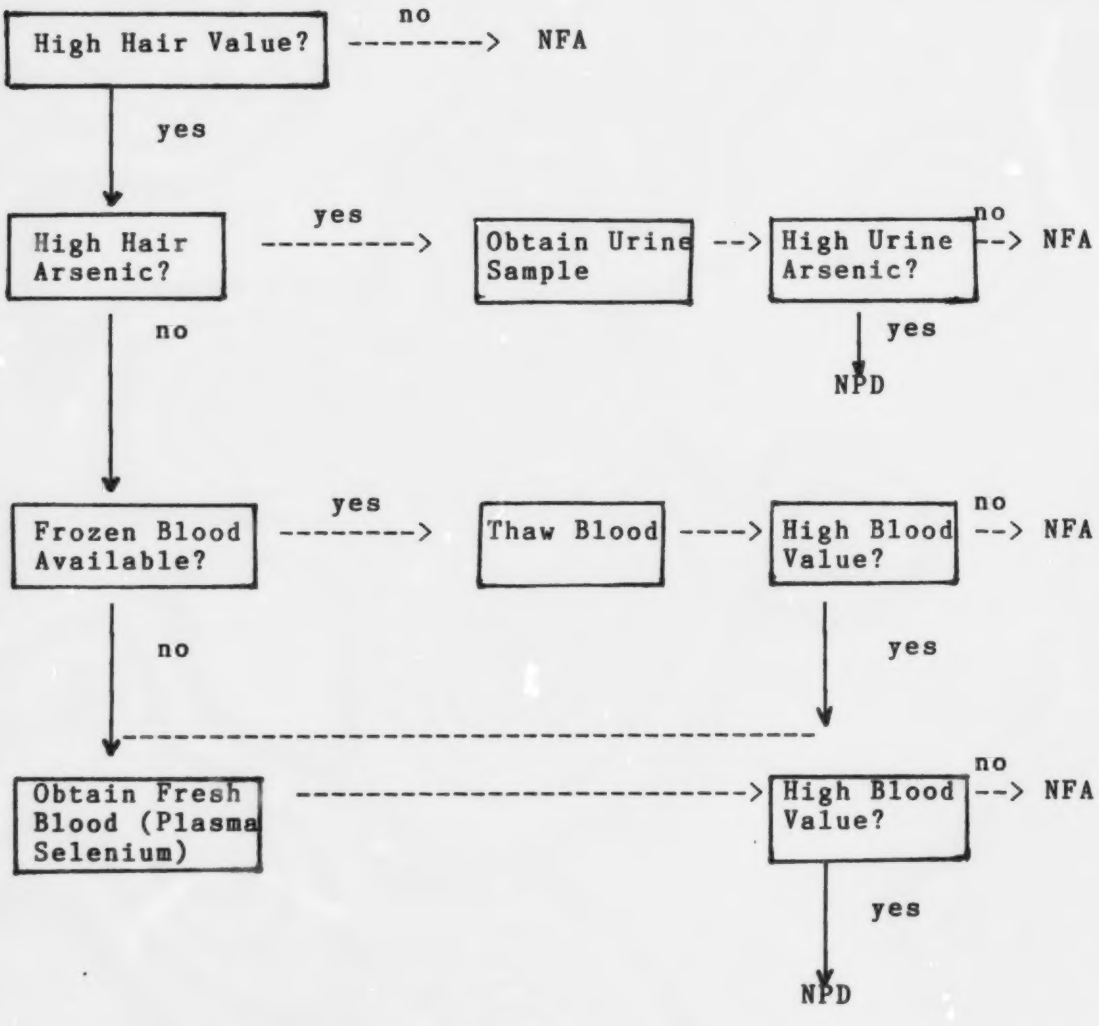
Threshold limits above which hair values were considered abnormal and/or of possible clinical importance were set through discussion with Dr. Jean-Phillipe Weber (Centre de Toxicologie du Quebec) and Dr. Tom Moyer (Mayo Clinic Laboratory). These limits were as follows; hair selenium or arsenic greater than 1 microgram per gram, hair cadmium or mercury greater than 5 micrograms per gram, and hair lead greater than 10 micrograms per gram.

As described earlier, hair values were done on all those with a sufficient amount of hair and blood mercury was done on all those at least 7 years of age. This blood sample once analyzed for mercury was stored, frozen at -80 degrees Celsius at the Centre de Toxicologie du Quebec laboratory.

The decision tree is shown in Figure I. If the hair arsenic was elevated the participant was contacted and asked to return for a urine sample. If other of the measured hair values were high the frozen blood sample in Quebec was thawed and the trace metals checked. Elevated blood levels were considered to be as follows: blood cadmium greater than 10 micrograms per litre in smokers and greater than 2 micrograms per litre in non-smokers, blood mercury greater than 20 micrograms per litre, blood lead greater than 200 micrograms per litre in children and greater than 300 micrograms per litre in adults, and serum/plasma selenium greater than 200 micrograms per litre. High measured values for cadmium in this sample could have been due to a cracked blood tube and high values for selenium because it was a whole blood sample. If no blood was available or the thawed blood had abnormal metal concentrations, a fresh sample was obtained during the winter study of 1986. If selenium was of concern, plasma samples were prepared. Those with confirmed high blood or urine values received notification with the necessary information to bring to their family physicians for follow-up.

Figure 1

Decision Tree for Dealing with Elevated Hair Trace Metals


High Hair Value?
no
NFA
yes
High Hair Arsenic?
yes
Obtain Urine Sample
High Urine Arsenic?
no
NFA
yes
NPD
no
Frozen Blood Available?
yes
Thaw Blood
High Blood Value?
no
NFA
no
yes
Obtain Fresh Blood (Plasma Selenium)
High Blood Value?
no
NFA
yes
NPD

NFA = No further action
NPD = Notification of participant and family doctor, who are responsible for any further action.

Appendix 14.3

DETAILED RESPIRATORY FUNCTION ANALYSIS

Appendix 14.3

DETAILED RESPIRATORY FUNCTION ANALYSIS

INTRODUCTION

In Volumes I and II of the main text, certain essential aspects of respiratory function were presented. These included respiratory symptoms, spirometry methods, methodological results, and results of FEV_1 measurement, the primary outcome variable. This appendix presents a more detailed account of respiratory function. Part I comprises respiratory symptoms, Part II illustrates the distributions of the spirometric variables, Part III describes in detail how spirometric results were adjusted for influencing factors, and Parts IV, V, VI, and VII contain the detailed analysis of FVC, MMEF, FEV_1/FVC, and bronchodilator response respectively.

Part I - Respiratory Symptoms

Tables 1/1 and 1/2 present the percentage of participants with respiratory symptoms among those who responded to the questionnaire for those 5-13 years of age and to the questionnaire for those at least 14 years of age. For both age groups, IA had a greater percentage than SR of participants with any respiratory symptoms, and DCCI had a greater percentage than SR-M. It is also important to note that IA had a greater percentage of symptoms than DCCI (a sour gas exposed comparison area). Also, the non-Mormon SR population was very similar to the overall SR population in terms of respiratory symptoms.

Part II - Distributions of Spirometric Variables Used to Indicate Lung Function

Figure 2/1 presents histograms of the logarithmic transformed FEV_1, MMEF, and FVC which were used to indicate lung function in children. It can be seen that they are well approximated by a normal distribution. Only for Log_e FVC was the distribution bimodal, probably due to girls 7-13 and boys 7-15 years old being included together. Figure 2/2 depicts the distribution of spirometric values used to indicate lung function in adults. Again, the shape is that of a normal distribution. Figure 2/3 demonstrates the distribution of adjusted FEV_1 values in adults by smoking status for each area. FEV_1 values were expressed as [(the largest observed FEV_1 - predicted FEV_1) ÷ (the standard deviation around the predicted regression line)]. The predicted values and standard deviations used were those of Knudson et al. (Am Rev Resp Dis, 1983;127:725). For each smoking group, the figures show the percentage of values on the ordinate represented by each mid-point on the abscissa. The distributions for each area by smoking status were not markedly different.

Figure 2/4 presents the distribution of adjusted FEV_1 values in children for each area. Again, distributions among the comparison areas appeared similar.

Figure 2/5 and 2/6 present the distribution of adjusted FEV_1/FVC values in children and adults using z-scores. For each participant the largest FEV_1 and largest FVC were used. Among children, and non-smoking adults the distributions among all areas were similar. Among currently smoking adults there appeared to be a slight relative excess of smaller values in SR as compared to other areas. Among former smokers, there appeared to be a slight relative excess of smaller values in IA as compared to other areas. To clarify the nature of this slight distribution variation, characteristics of those individuals with z-scores less than -6 were checked: all 8 individuals were males 62-77 years of age of whom 6 resided in IA. Apart from one non-smoker, all had smoked from 24.5 to 68.8 pack-years (8,942 to 25,185 packages of cigarettes).

Figure 2/7 demonstrates the distribution of percentage bronchodilator response for all participants by area. Bronchodilator response to a single inhalation of terbutaline was measured as [((largest FEV_1 post-bronchodilator - largest FEV_1 pre-bronchodilator)/largest FEV_1 pre-bronchodilator) X 100]. The distributions for each area appeared similar with the modal value at the 2% mid-point.

It is important to note that on average, externally adjusted FVC values will tend to be greater than 100% of predicted and MMEF values less than 100% predicted. This is because the testing technique used for the present study was different from that used to develop the equations which we used for reference. This would not be expected to influence comparisons between areas in the present study. An additional factor important to interpretation of results is the intra-seasonal variation discussed in section 9.8. It suggests that the true mean FVC may have been underestimated by about a 0.5% and MMEF overestimated by 1% in IA relative to SR.

Part III - The Method of Internal Adjustment of Spirometric Results

For each sex, a multivariate model was tested to explain pulmonary function over all ages. However, plotting residuals of these spirometric variables against height revealed a marked inhomogeneity of variance. Residuals were closely clustered to a height of approximately 160-165 cm. at which time they abruptly spread out. Results were then separated into two age groups, children and adults, for each sex at the point where the growth phase slowed, i.e. where age and height lost their close correlation. The younger group corresponded to ages in females from 7-13 years inclusive and for males 7-15 years inclusive. For each age-sex group, the linear, quadratic, or logarithmic combinations of age, height and weight which best explained variation in FEV_1, FVC, and MMEF were assessed. It was found that in general 2 to 3 variable combinations explained as much variance in each dependent variable as 6 to 7 variable combinations within 1% of R^2. A combination of the smallest number of variables explaining within 2% of the maximum variation explained by larger combinations was chosen. Where possible, combinations, which for any age-group used the same term for both sexes were selected. Sexes within each age-group were then combined and centered interaction terms were assessed. Residuals in the first age-group demonstrated gradually increasing inhomogeneity of variance from younger to older age which was corrected by taking the natural logarithm of the dependent variables FEV_1, FVC, and MMEF. In the second age-group, inhomogeneity of variance with age was not evident. Following this, the technician and spirometer responsible for each test result were added to the models in both age-groups. Spirometer used did not explain any variation in the dependent variables ($p < .05$) with technician in the model. In adults, the technician variable contributed significantly ($p < .001$) to explaining variation in adult FVC and MMEF and thus was left in these models. For children an area*age interaction term was significant for FEV_1 ($p = .007$) and MMEF ($p = .0004$). To demonstrate the interaction in tabular form, children's lung function is presented stratified by 2-3 year periods. For adults, neither area nor age*area interaction was found.

Part IV - FVC Results

Tables 4/1 and 4/2 present FVC values for children and adults respectively. Results are presented as unadjusted values and values both externally adjusted and internally adjusted as described in the main text and in the footnotes to these tables. Children in IA had greater unadjusted lung function values than children in the SR; these differences persisted when the results were internally adjusted and externally adjusted. DCCI as compared to SR-M showed lower unadjusted values, but slightly greater internally adjusted and externally adjusted values. Summarizing the findings for FVC in children, IA was consistently higher than SR and DCCI was not consistently better or worse than SR-M. Among adults, IA as compared to SR showed higher unadjusted FVC values in smokers and lower unadjusted values in non-smokers. Internally and externally adjusted values were similar between IA and SR. DCCI as compared to SR-M showed similar unadjusted FVC values for men and somewhat lower unadjusted values for women. Internally adjusted and externally adjusted values were similar between IA and SR.

Part V - MMEF Results

As shown in Table 5/1, children in IA as compared to SR showed larger unadjusted MMEF values for both sexes and these differences persisted after both external and internal adjustment. For DCCI as compared to SR-M, MMEF results before adjustment and after internal adjustment tended to be lower; after external adjustment results were similar. Summarizing MMEF results for children, IA had consistently greater results than SR, and DCCI was very similar to SR-M with a tendency, less than one standard error difference, to have smaller values. Among adults, for IA as compared to SR, unadjusted results tended to be lower while both internally and externally adjusted results were similar (Table 5/2). For DCCI as compared to SR-M, unadjusted values, as well as internally and externally adjusted values tended to be lower.

Part VI - (100 x FEV_1/FVC) Results

The composite variable, (100 X FEV_1/FVC), was previously presented in Volume 2 Table 13.4.1.3/2 in a crude form unadjusted for differences between areas in age, sex, and smoking which influence results. Among these participants $\geq$ 15 years with data available for use in the clinical algorithms, there was a 2.0% difference favoring IA over SR in the percentage of those with $(100 \times FEV_1/FVC) < 70\%$.

This small difference was not statistically significant ($p = .28$ using a chi-square test) but the Scientific Advisory Board used this crude value in part to form conclusions in their June 3, 1986 report. Thus, to clarify the issue, the variable was put in this section where it could be discussed and undergo accurate analyses, adjusting for factors which could bias and reduce the precision of crude comparisons. It will be shown that there was a trend for IA children to have a slightly better (FEV_1/FVC) value than SR, and IA adults to have (FEV_1/FVC) values similar to SR adults.

Tables 6/1 and 6/2 present $(100 \times FEV_1/FVC)$ results for children and adults respectively. Results are presented as unadjusted values and values both externally and internally adjusted as described previously. Children in IA had greater unadjusted values than children in SR. These differences persisted when the results were internally adjusted and externally adjusted. Children in DCCI had greater unadjusted lung function values than children in SR-M; these differences also persisted when the results were internally and externally adjusted. Among adults, IA as compared to SR showed lower unadjusted results, similar externally adjusted results and slightly better internally adjusted results. DCCI as compared to SR-M showed slightly lower unadjusted results, similar externally adjusted results and externally adjusted results and somewhat lower internally adjusted results.

Thus, for FEV_1/FVC results, among children there was a trend for IA to show more favourable results than SR, and DCCI to show slightly more favourable results than SR-M. Among adults there was no consistent trend between IA and SR and DCCI had slightly less favourable results than SR-M. All differences were however very small.

This FEV_1/FVC ratio was dichotomized into low (< 70%) and high ratios. As seen in Table 6/3, the crude difference in the proportion of adults with a low ratio between IA and SR is 2%, while for children it is -1%. These differences were adjusted for the potentially confounding effect of age, sex, height, weight, smoking (current and cumulative in adults only), spirometer and FVC. As seen in Table 6/3, the adjustments have only a minimal impact: the differences become 1.1% and -3.6%, respectively for adults and children and are not statistically significant.

Part VII - The Influence of Bronchodilator Responsiveness on the Relationship Between FEV_1 and Area

The rationale for measuring bronchodilator responsiveness was that it could perhaps identify a sub-group of individuals with increased sensitivity to environmental pollutants. Such sensitive individuals may show effects not seen in the general study population. Percentage bronchodilator response was defined as: [((Best FEV_1 Post-Bronchodilator - Best FEV_1 Pre-Bronchodilator)/Best FEV_1 Pre-Bronchodilator) X 100]. The bronchodilator used was 250 ug. of terbutaline in children aged 7-12 years old and 500 mg. of terbutaline in older individuals. The aerosol was administered using a 750 ml. spacer and the post-bronchodilator response was measured 20 minutes following administration. Responsiveness was dichotomized as increased if the percentage response was $\geq$ the top decile of response in the overall study group. This value corresponded to $\geq$ to the 7.4% for children and $\geq$ 7.3% for adults.

Table 7/1 shows differences in lung function by area between those with an increased bronchodilator response and those without an increased response. For IA as compared to SR, those with an increased response showed differences in lung function similar to those without an increased response. For DCCI as compared to SR-

M, those with an increased response tended to have better lung function in DCCI as compared to SR-M, slightly different and opposite in direction to those without an increased response.

The percentage bronchodilator response was previously presented in Volume 2 Table 13.4.1.3/2 in a crude form unadjusted for influencing variables. Among those participants $\geq$ 15 years with data available for use in the clinical algorithms, there was a 2.1% difference favoring SR over IA in the percentage with a response > 7.7%. This small difference was not statistically significant ($p > .1$) but the Scientific Advisory Board used this crude value in part to reach conclusions in their June 3, 1986 report. Thus, to clarify this issue, it was put in this section where it could undergo careful analysis adjusting for factors which could bias and reduce the precision of crude comparisons.

As shown in Table 7/1 children in IA as compared to SR showed smaller (probably more favourable) unadjusted bronchodilator responses and this difference persisted after internal adjustment. Unadjusted and adjusted values were smaller in DCCI as compared to SR-M.

Among adults, for IA as compared to SR, the unadjusted and adjusted values were similar. DCCI tended to have lower unadjusted and adjusted values than SR-M. However all adult differences were small.

The percentage bronchodilator response was also dichotomized into high (> 7.7%) and low. As seen in Table 7/3, the crude difference in the proportion of adults with a high percentage (< 7.7%) between IA and SR is 2.7%, and -8.4% in children. These differences were adjusted for the potentially confounding effect of age, sex, height, weight, smoking (current and cumulative for adults only) and spirometer. As seen in Table 7/3, the adjustments have a slight inpact favoring IA: the differences become 0.3% and -12.4% respectively for adults and children. The difference for adults is not statistically significant while the difference for children is statistically significant favouring IA children.

TABLE 1/1

PERCENTAGE OF PARTICIPANTS 5 TO 13 YEARS OF AGE WITH RESPIRATORY SYMPTOMS AS REPORTED BY QUESTIONNAIRE

	AREA			
Symptom	IA	SR	DCCI	SR-M
N	488	203	152	125
Persistent Cough (21C)*	10	02	07	03
Persistent Phlegm (22B)	06	02	03	02
Wheeze Following Exertion (26)	07	06	09	05
Persistent Wheeze (24B)	06	06	08	06
Episodes of Wheeze with Dyspnea (25B)	13	10	14	09
Exertional Dyspnea (11L)	02	01	01	02
Chest Illness Requiring Hospitalization (27)	19	11	10	09
Any of the Above Symptoms	32	21	25	19

* Question number that elicited the positive response.

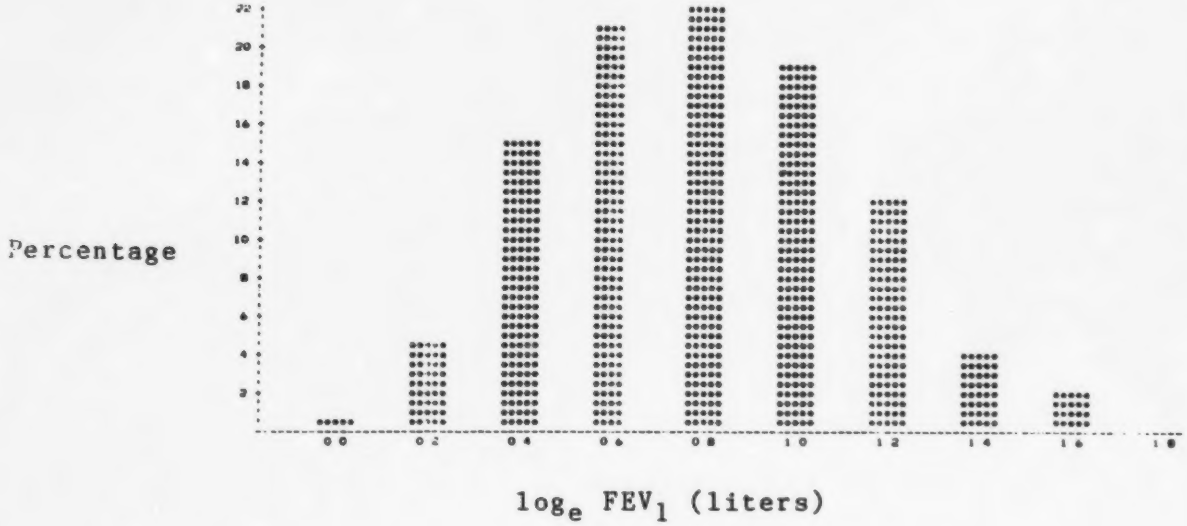
TABLE 1/2

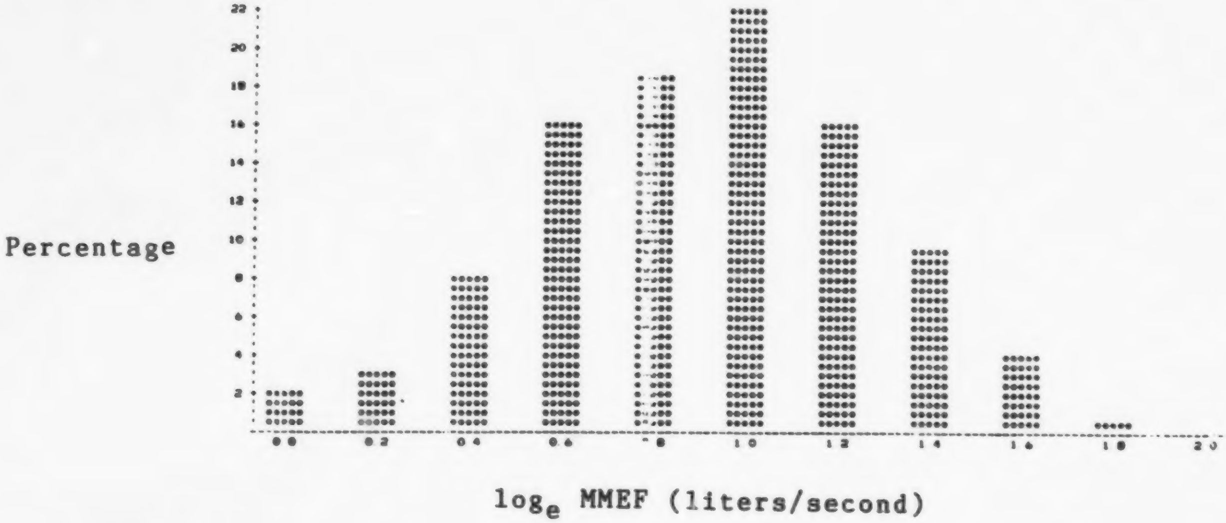
PERCENTAGE OF PARTICIPANTS AT LEAST 14 YEARS OF AGE WITH RESPIRATORY SYMPTOMS AS REPORTED BY QUESTIONNAIRE

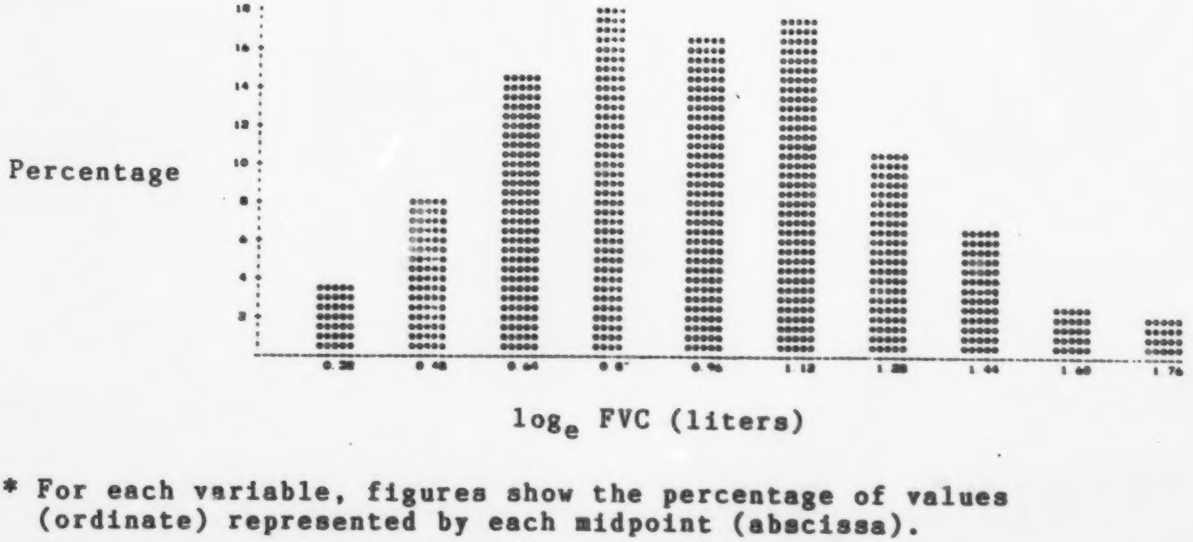
		AREA			
Symptom	Smoking Status	IA	SR	DCCI	SR-M
N		1429	509	372	303
Persistent Cough (22E)*	current	38	36	41	33
	ex	11	05	05	07
	never	08	04	08	04
Persistent Phlegm (23E)	current	29	28	27	26
	ex	15	08	10	11
	never	11	04	07	03
Persistent Wheeze (24A-3)	current	23	26	25	23
	ex	13	10	06	07
	never	07	04	05	03
Episodes of Wheeze with Dyspnea (25C)	current	18	11	12	10
	ex	15	10	14	09
	never	09	08	08	09
Exertional Dyspnea (26B)	current	10	11	08	08
	ex	09	05	05	04
	never	07	05	05	06
Chest Illness Preventing Work (27)	current	21	12	15	13
	ex	17	08	14	07
	never	19	13	14	11
Any of the Above Symptoms	current	64	61	67	60
	ex	43	33	32	32
	never	38	28	30	28

* Question number that elicited the positive response.

Figure 2/1 DISTRIBUTIONS OF THE SPIROMETRIC VARIABLES USED TO INDICATE LUNG FUNCTION IN CHILDREN*

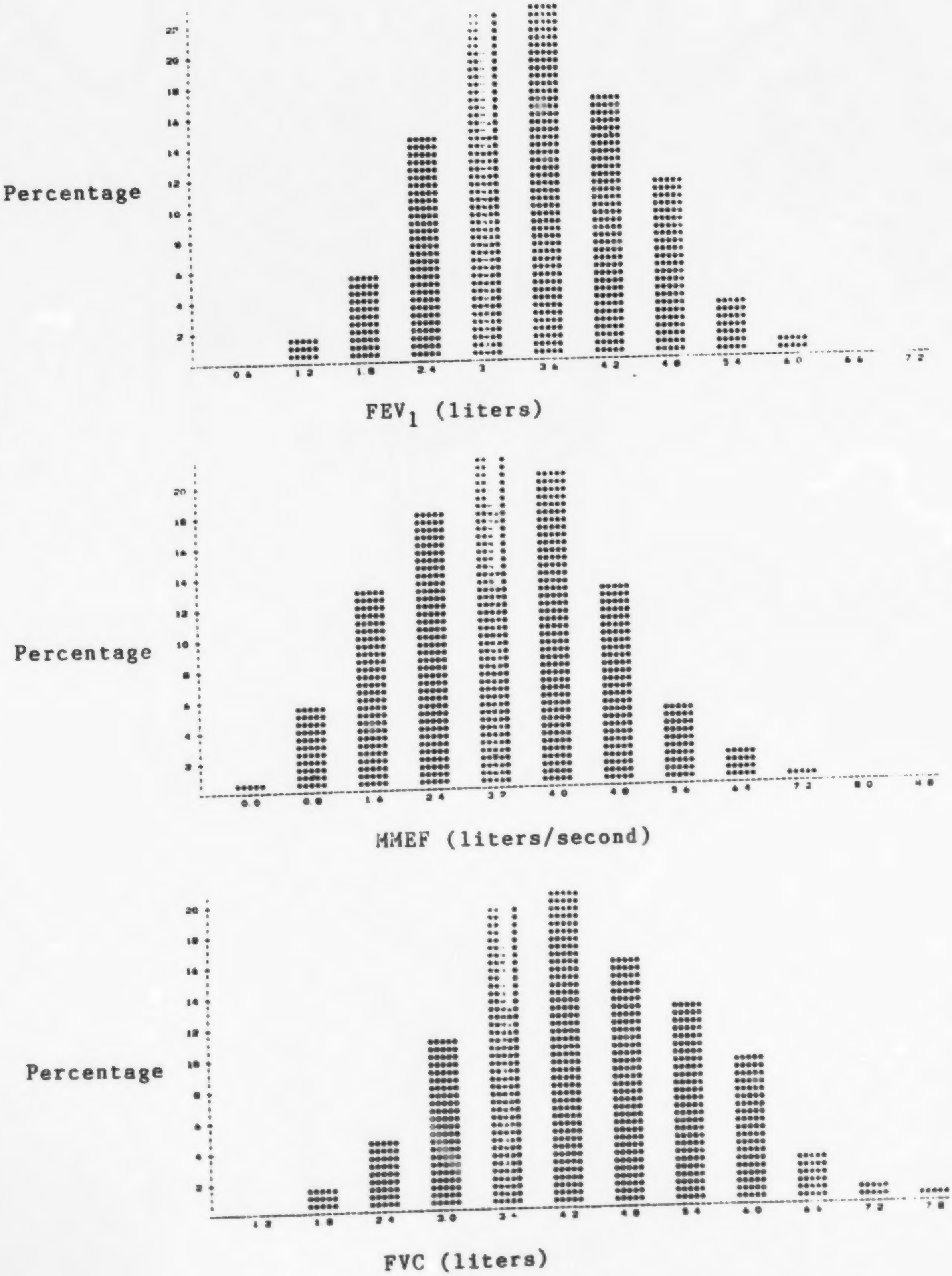






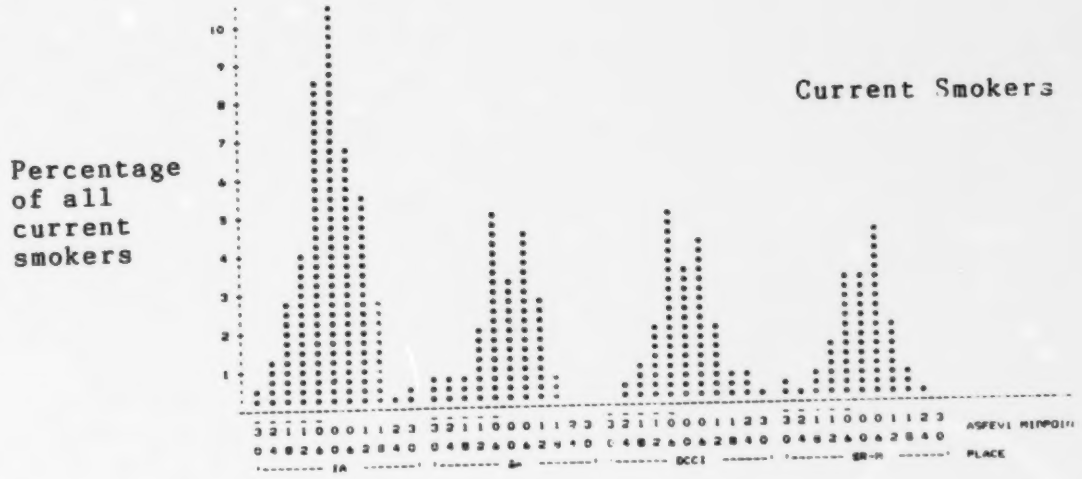
* For each variable, figures show the percentage of values (ordinate) represented by each midpoint (abscissa).

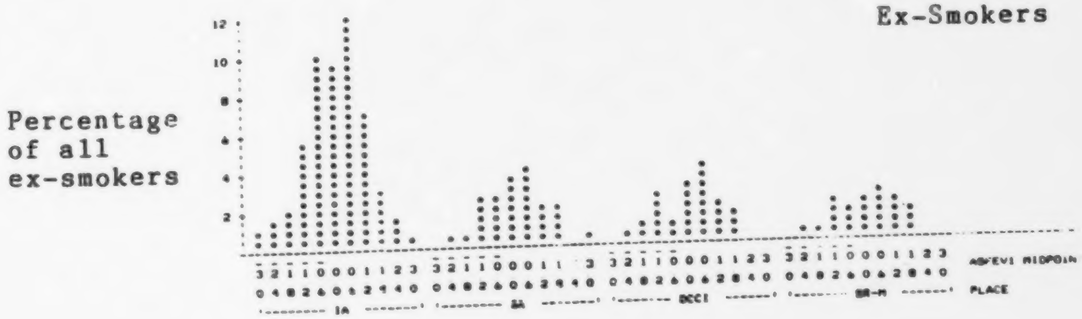
Figure 2/2 DISTRIBUTIONS OF THE SPIROMETRIC VARIABLES USED TO INDICATE LUNG FUNCTION IN ADULTS*

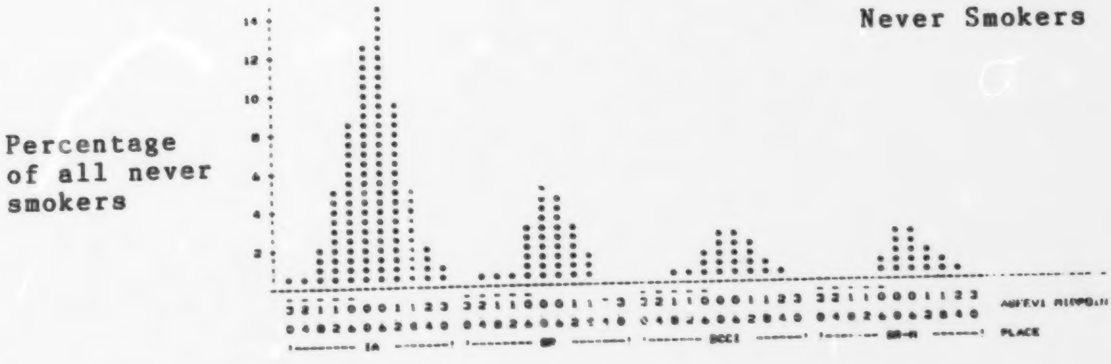


* For each variable, figures show the percentage of values (ordinate) represented by each midpoint (abscissa).

Figure 2/3 DISTRIBUTIONS OF ADJUSTED FEV$_1$ VALUES IN ADULTS BY SMOKING STATUS FOR EACH AREA*



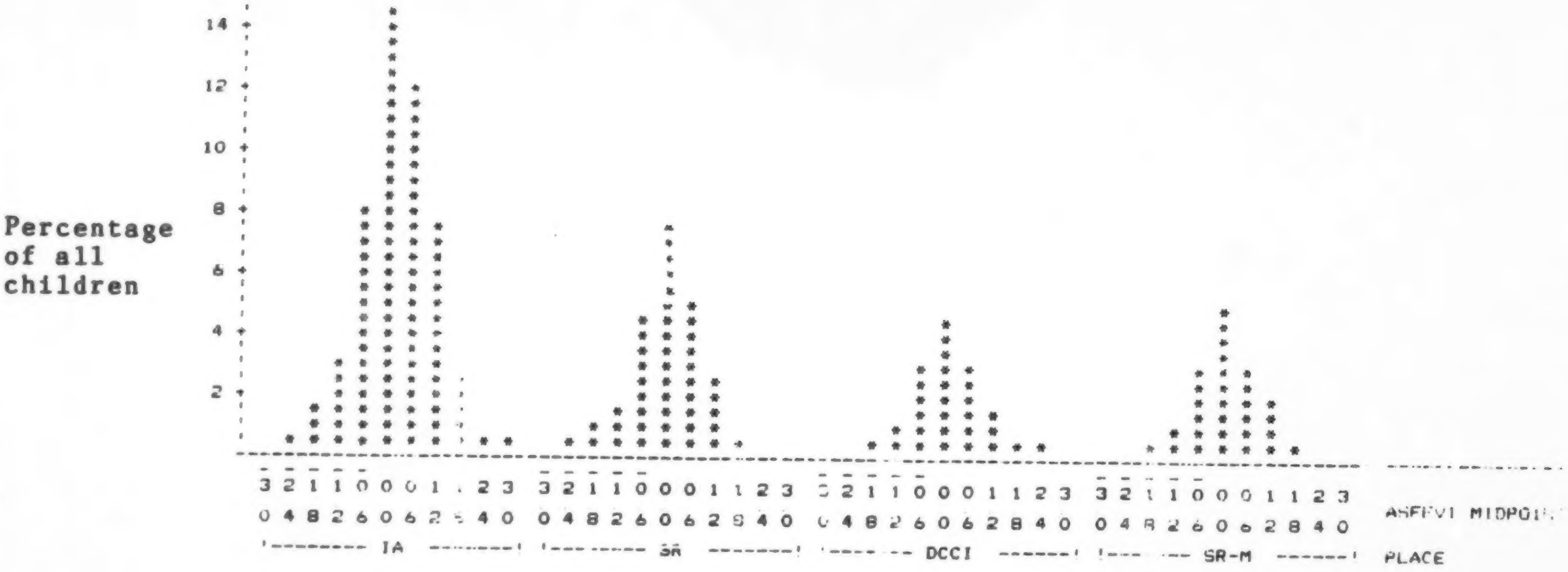




* FEV$_1$ values are expressed as (largest FEV$_1$ observed - predicted FEV$_1$)/standard deviation around predicted regression line. Predicted values and standard deviation are those of Knudson et al., Am Rev Resp Dis 1983;127:725. For each smoking group, figures show the percentge of values (ordinate) represented by each adjusted FEV$_1$ midpoint (abscissa). Note that numbers written on abscissa are written vertically.

Figure 2/4

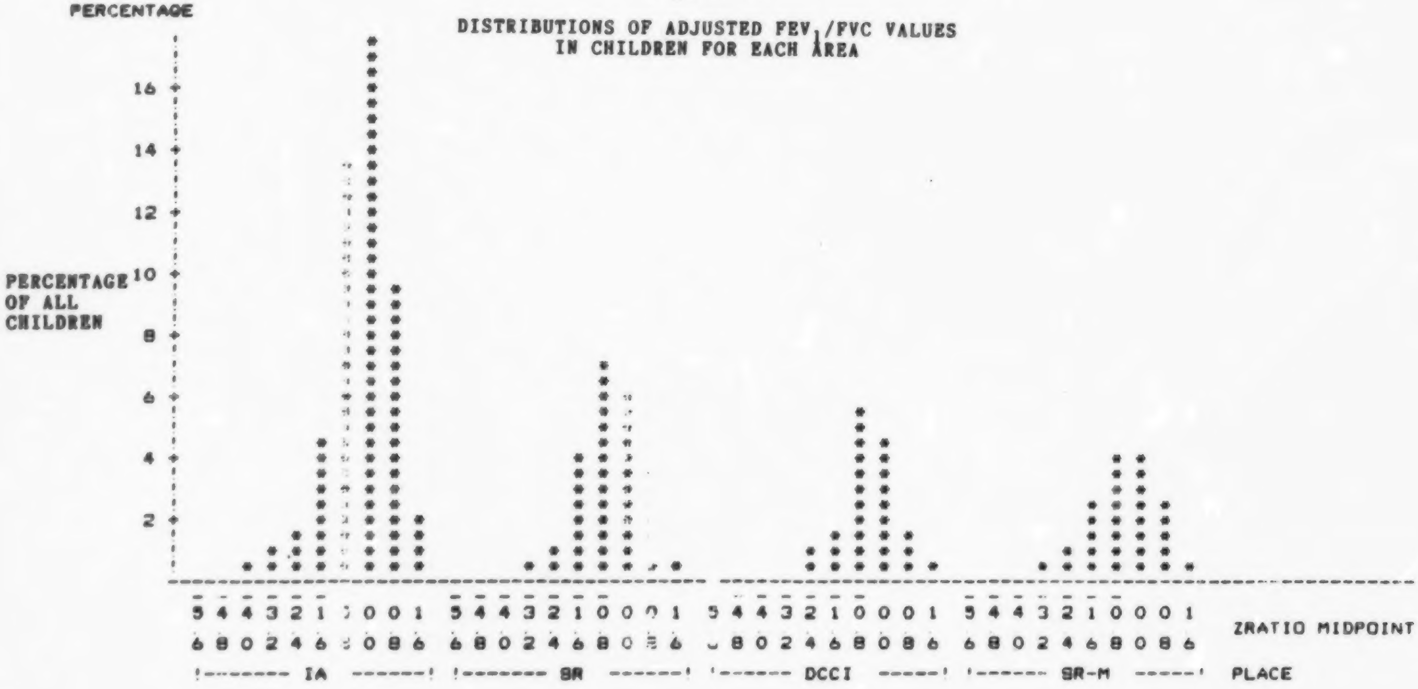
DISTRIBUTION OF ADJUSTED FEV$_1$ VALUES
IN CHILDREN FOR EACH AREA*



* FEV$_1$ values are expressed as (largest FEV$_1$ observed - predicted FEV$_1$)/standard deviation around predicted regression line. Predicted values and standard deviation are those of Knudson et al., Am Rev Resp Dis 1983;127:725. Figure shows the percentage of values (ordinate) represented by each adjusted FEV$_1$ midpoint (abscissa). Note that numbers on abscissa are written vertically.

Figure 2/5

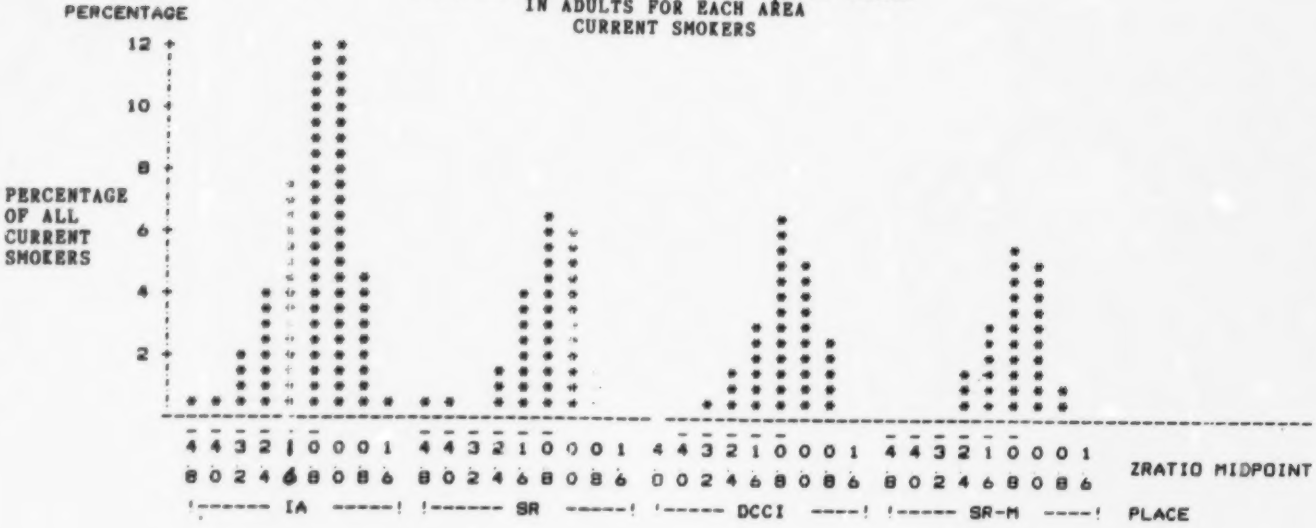
DISTRIBUTIONS OF ADJUSTED FEV_1/FVC VALUES IN CHILDREN FOR EACH AREA



* FEV_1/FVC values are expressed as (largest FEV_1/FVC observed - predicted FEV_1/FVC)/standard deviation around predicted regression line. Predicted values and standard deviation are those of Knudson et al., Am Rev Resp Dis 1983;127:725. Figure shows the percentage of values (ordinate) represented by each midpoint (abscissa).

Figure 2/6 (1)

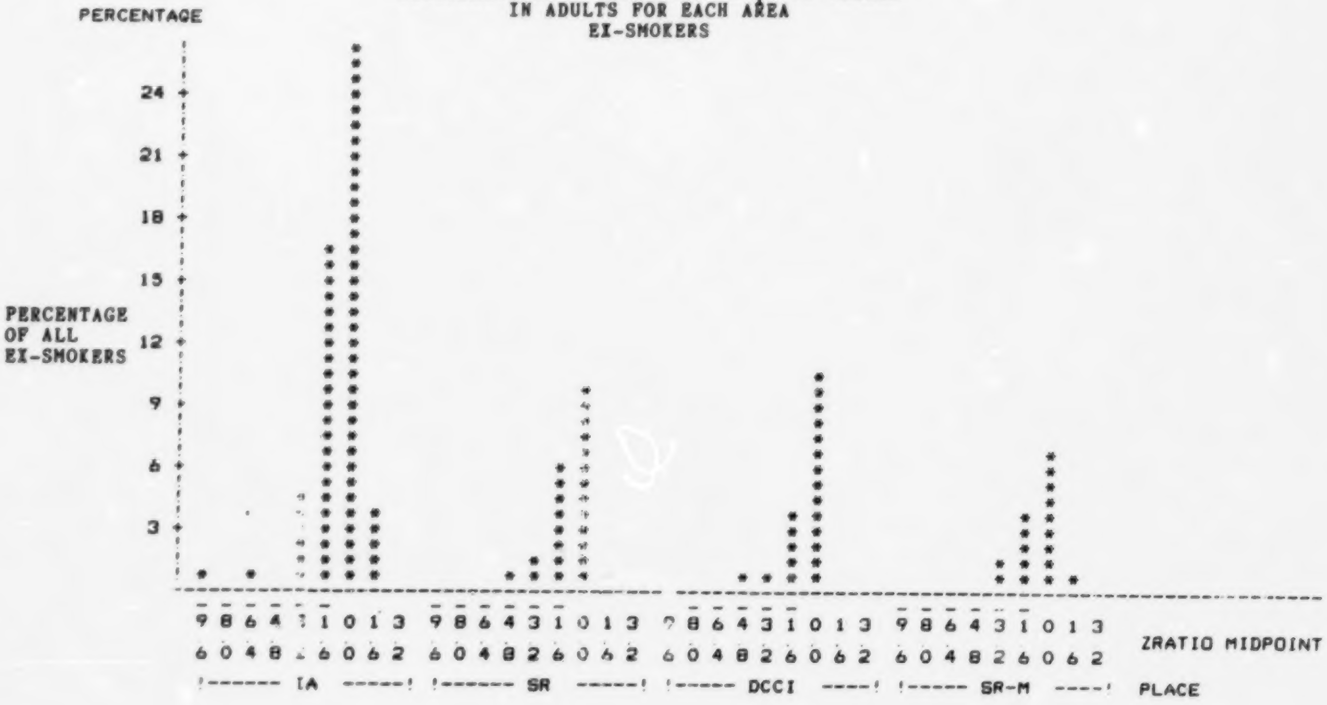
DISTRIBUTIONS OF ADJUSTED FEV_1/FVC VALUES
IN ADULTS FOR EACH AREA
CURRENT SMOKERS



* FEV_1/FVC values are expressed as (largest FEV_1/FVC observed - predicted FEV_1/FVC)/standard deviation around predicted regression line. Predicted values and standard deviation are those of Knudson et al., Am Rev Resp Dis 1983;127:725. For each smoking group, figures show the percentage of values (ordinate) represented by each midpoint (abscissa).

Figure 2/6 (2)

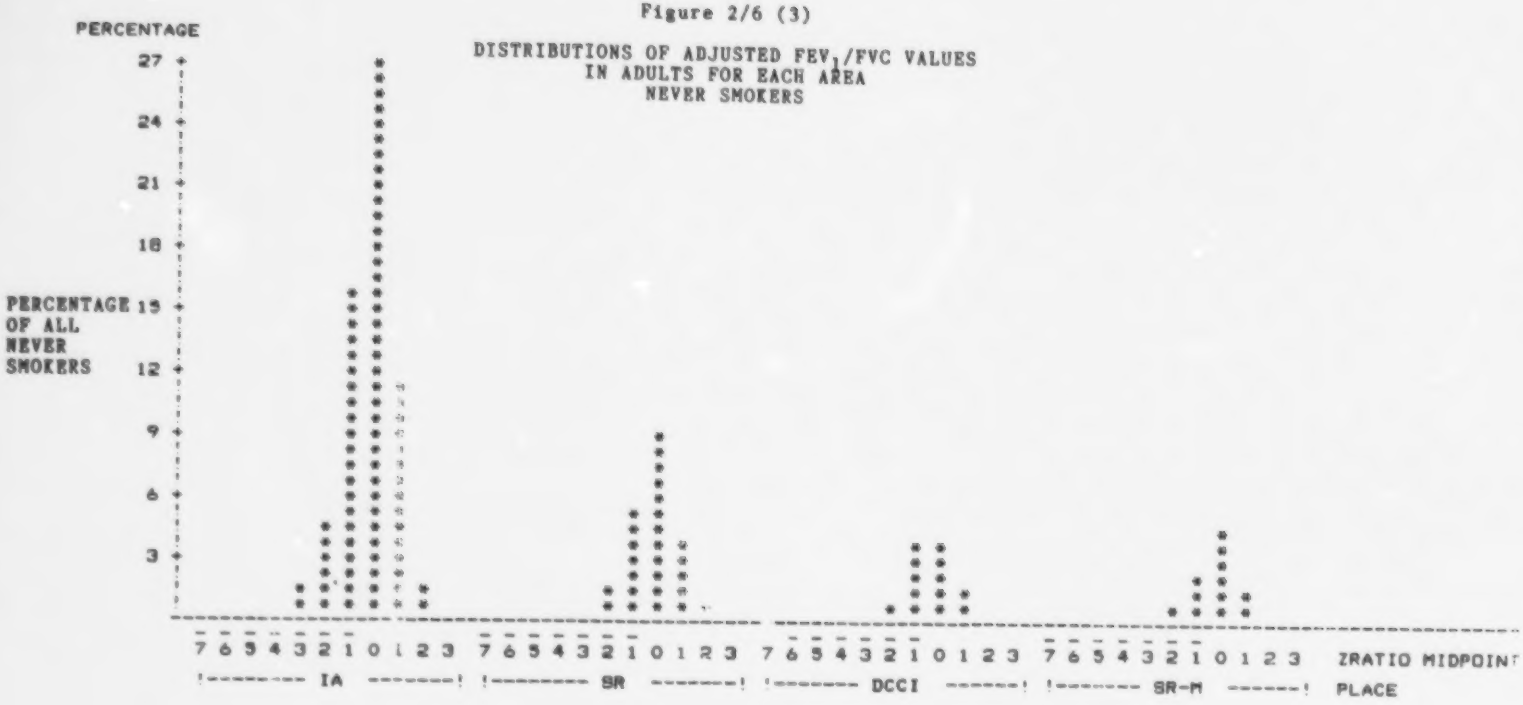
DISTRIBUTIONS OF ADJUSTED FEV$_1$/FVC VALUES
IN ADULTS FOR EACH AREA
EX-SMOKERS



* FEV$_1$/FVC values are expressed as (largest FEV$_1$/FVC observed - predicted FEV$_1$/FVC)/standard deviation around predicted regression line. Predicted values and standard deviation are those of Knudson et al., Am Rev Resp Dis 1983;127:725. For each smoking group, figures show the percentage of values (ordinate) represented by each midpoint (abscissa).

Figure 2/6 (3)

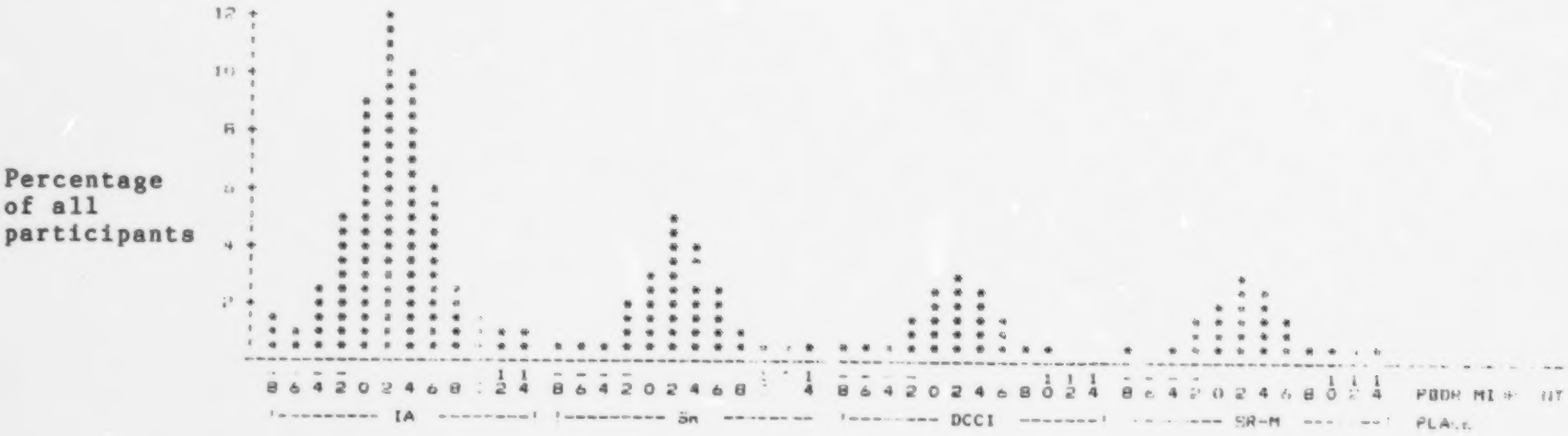
DISTRIBUTIONS OF ADJUSTED FEV$_1$/FVC VALUES
IN ADULTS FOR EACH AREA
NEVER SMOKERS



* FEV$_1$/FVC values are expressed as (largest FEV$_1$/FVC observed - predicted FEV$_1$/FVC)/standard deviation around predicted regression line. Predicted values and standard deviation are those of Knudson et al., Am Rev Resp Dis 1983;127:725. For each smoking group, figures show the percentage of values (ordinate) represented by each midpoint (abscissa).

Figure 2/7

DISTRIBUTION OF PERCENTAGE BRONCHODILATOR RESPONSE
FOR ALL PARTICIPANTS BY AREA*



* Bronchodilator response to a single inhalation of terbutaline was measured as [((largest FEV_1 post-bronchodilator - largest FEV_1 pre-bronchodilator)/largest FEV_1 pre-bronchodilator) X 100]. Figure shows the percentage of values (ordinate) for each midpoint (abscissa). Note that numbers on the abscissa are written vertically.

TABLE 4/1

FVC MEASUREMENTS IN CHILDREN BY AREA*

FVC by Sex and Age	Number	AREA			
		IA	SR	DCCI	SR-M
Boys N		236	97	57	67
Unadjusted values					
7-9 years	147	2.09	1.96	2.05	1.93
10-11 years	89	2.72	2.65	2.74	2.73
12-13 years	98	3.45	3.55	3.76	3.66
14-15 years	56	4.52	4.53	3.80	4.79
all ages	390	2.95	2.94	2.75	3.03
		(0.07)	(0.11)	(0.11)	(0.14)
Girls N		160	81	53	49
Unadjusted values					
7-9 years	115	1.92	1.55	1.62	1.57
10-11 years	100	2.60	2.53	2.55	2.59
12-13 years	79	3.19	3.27	3.12	3.24
all ages	294	2.47	2.46	2.49	2.49
		(0.05)	(0.07)	(0.10)	(0.13)
Boys and Girls					
Unadjusted values	684	2.76	2.72	2.62	2.80
		(0.05)	(0.07)	(0.08)	(0.09)
Adjusted (internal)**					
7-9 years	262	2.55	2.49	2.54	2.44
10-11 years	189	2.63	2.58	2.55	2.60
12-13 years	177	2.60	2.62	2.61	2.65
14-15 years	56	2.72	2.62	2.81	2.72
all ages	684	2.62	2.58	2.63	2.60
Adjusted (external)***					
% predicted	684	104.3	103.2	104.3	103.7
		(0.6)	(0.8)	(1.2)	(1.0)

* Children were defined as those females 7 to 13 years of age, and those males 7 to 15 years of age inclusive. Table shows mean (standard error) in litres.

** The association between FVC and area was estimated using the equation of the form: $\log_e$ (FVC) = age, sex, height, $\log_e$ (weight), area, area*age ($R^2 = 0.90$). The data are presented by using age-area specific least squares FVC means taken at the mean values of sex, height, and $\log_e$ (weight).

*** Actual values expressed as a percentage of predicted by equations of Knudson et al. 1983 which take into account sex, age, and height.

TABLE 4/2
FVC MEASUREMENTS IN ADULTS BY AREA*

FVC by Sex and Smoking Status		Percentage	AREA			
			IA	SR	DCCI	SR-M
Men N			678	245	157	148
Unadjusted values						
Smoking:	current	20	5.21	5.01	5.26	5.02
	ex	25	5.05	4.98	5.02	4.90
	never	56	5.11	5.18	5.08	5.33
	all	100%	5.10	5.11	5.12	5.12
			(0.04)	(0.06)	(0.08)	(0.07)
Women N			700	230	169	132
Unadjusted values						
Smoking:	current	18	3.80	3.76	3.76	3.84
	ex	11	3.86	3.82	3.49	3.86
	never	71	3.64	3.70	3.61	3.78
	all	100%	3.68	3.73	3.62	3.81
			(0.03)	(0.05)	(0.06)	(0.06)
Men and Women N			1378	475	326	280
Unadjusted values			4.38	4.44	4.34	4.50
			(0.03)	(0.05)	(0.06)	(0.06)
Adjusted (internal)**			4.42	4.40	4.46	4.44
			(0.02)	(0.03)	(0.03)	(0.03)
Adjusted (external)*** by smoking status	% predicted					
	current	18	108.1(1.0)	106.6(1.5)	108.0(1.3)	108.7(1.6)
	ex	18	108.6(1.0)	110.1(1.8)	107.3(1.7)	110.0(2.1)
	never	63	107.8(0.5)	108.8(0.8)	109.7(1.1)	110.6(1.1)
		100%				

* Adults were defined as those females at least 14 years of age and those males at least 16 years of age. Table shows mean (standard error) in litres.

** The association between FVC and area was estimated using the equation of the form FVC = sex, age, $\log_e$ (age), height, current number of cigarettes smoked daily, number of cigarettes smoked over lifetime, technician, area ($R^2 = 0.76$). The data are presented by using area specific least squares FVC means taken at the mean values of the covariates.

*** Actual value expresed as a percentage of value predicted by equations of Knudson et al. 1983 which take into account, sex, age, and height.

TABLE 5/1

MMEF MEASUREMENTS IN CHILDREN BY AREA*

MMEF by Sex and Age	Number	AREA			
		IA	SR	DCCI	SR-M
Boys N		236	97	57	67
Unadjusted values					
7-9 years	147	2.19	1.78	1.85	1.73
10-11 years	89	2.49	2.13	2.28	2.17
12-13 years	98	2.98	3.18	3.44	3.19
14-15 years	56	4.29	4.20	3.52	4.38
all ages	390	2.79	2.61	2.44	2.66
		(0.07)	(0.12)	(0.12)	(0.15)
Girls N		160	81	53	49
Unadjusted values					
7-9 years	115	2.04	1.66	2.03	1.76
10-11 years	100	2.69	2.64	2.43	2.75
12-13 years	79	3.40	3.32	3.03	3.29
all ages	294	2.60	2.45	2.49	2.53
		(0.07)	(0.10)	(0.10)	(0.13)
Boys and Girls					
Unadjusted values	684	2.71	2.54	2.46	2.60
		(0.05)	(0.08)	(0.08)	(0.10)
Adjusted (internal)**					
7-9 years	262	2.05	1.66	1.91	1.68
10-11 years	189	2.49	2.29	2.28	2.38
12-13 years	177	3.02	3.17	3.05	3.15
14-15 years	56	3.82	3.65	3.45	3.79
all ages	684	2.77	2.57	2.60	2.63
Adjusted (external)***					
% predicted	684	100.4	92.9	94.1	93.8
		(1.2)	(1.8)	(1.9)	(2.2)

* Children were defined as those females 7 to 13 years of age, and those males 7 to 15 years of age inclusive. Table shows mean (standard error) in litres/second.

** The association between MMEF and area was estimated using the equation of the form: $\log_e$ (MMEF) = age, sex, height^2, sex*height^2 area, area x age. (R^2 = 0.49). The data are presented by using the age-area specific least squares MMEF means taken at the mean values of sex and height^2.

*** Actual values expressed as a percentage of predicted by equations of Knudson et al. 1983 which take into account sex, age, and height.

TABLE 5/2

MMEF MEASUREMENTS IN ADULTS BY AREA*

MMEF by Sex, and Smoking Status		Percentage	AREA			
			IA	SR	DCCI	SR-M
Men N			678	245	157	148
Unadjusted values						
Smoking:	current	20	3.49	3.36	3.63	3.33
	ex	25	3.12	3.22	3.27	3.17
	never	56	3.83	4.10	3.61	4.31
	all	100%	3.59 (0.06)	3.75 (0.09)	3.53 (0.1)	3.72 (0.1)
Women N			700	230	169	132
Unadjusted values						
Smoking:	current	18	2.75	2.93	2.68	2.93
	ex	11	3.16	3.03	2.94	3.26
	never	71	3.05	3.09	2.80	3.14
	all	100%	3.02 (0.04)	3.05 (0.07)	2.78 (0.09)	3.09 (0.09)
Men and Women N			1378	475	326	280
Unadjusted values			3.30 (0.04)	3.41 (0.06)	3.14 (0.08)	3.42 (0.08)
Adjusted (internal)**			3.28 (0.04)	3.28 (0.05)	3.23 (0.06)	3.33 (0.06)
Adjusted (external)*** by smoking status	% predicted					
	current	18	79.8(2.0)	80.9(2.9)	80.2(2.8)	81.4(3.0)
	ex	18	81.6(2.0)	83.5(3.3)	86.5(3.6)	83.9(4.3)
	never	63	92.8(0.9)	93.9(1.5)	87.5(2.3)	96.3(2.2)
		100%				

* Adults were defined as those females at least 14 years of age and those males at least 16 years of age. Table shows mean (standard error) in litres.

** The association between MMEF and area was estimated using the equation of the form MMEF = sex, age, height^2, age x height^2, sex x height^2, current number of cigarettes smoked daily, number of cigarettes smoked over lifetime, technician, area ($R^2 = 0.55$). The data are presented using the area specific least squares MMEF means taken at the mean values of the covariates.

*** Actual value expresed as a percentage of value predicted by equations of Knudson et al. 1983 which take into account, sex, age, and height.

TABLE 6/1
(100 X FEV_1/FVC) MEASUREMENTS IN CHILDREN BY AREA*

	AREA			
FEV_1/FVC by sex	IA	SR	DCCI	SR-M
Boys N	236	97	57	67
unadjusted	85.6 (0.4)	83.4 (0.6)	84.2 (0.7)	83.3 (0.7)
adjusted (external) percent predicted	96.7 (0.5)	94.2 (0.7)	94.7 (0.8)	94.1 (0.8)
z-score	-0.46 (0.06)	-0.80 (0.10)	-0.73 (0.11)	-0.80 (0.11)
Girls N	160	81	53	49
unadjusted	88.1 (0.4)	86.1 (0.7)	86.5 (0.7)	86.5 (1.0)
adjusted (external) percent predicted	100.3 (0.5)	97.8 (0.9)	98.2 (0.8)	98.5 (1.2)
z-score	0.02 (0.07)	-0.29 (0.12)	-0.25 (0.10)	-0.20 (0.15)
Boys and Girls				
unadjusted	86.6 (0.3)	84.6 (0.5)	85.3 (0.5)	84.6 (0.6)
adjusted (external) percent predicted	98.1 (0.4)	95.8 (0.6)	96.4 (0.6)	96.0 (0.7)
z-score	-0.26 (0.05)	-0.57 (0.08)	-0.50 (0.08)	-0.55 (0.10)
internally adjusted	85.9 (0.4)	83.8 (0.5)	84.4 (0.6)	83.8 (0.6)

---

* Boys were 7-15 years of age inclusive and girls 7-13 years of age inclusive. Percent predicted = unadjusted value expressed as a percent of predicted by the equations of Knudson et al. 1983. z-score = [(unadjusted value - predicted value)/standard deviation around regression line] using equation of Knudson for predicted and standard deviation values. Standard error is presented in parentheses. For internal adjustment the association between (FEV_1/FVC) and area was estimated using the equation of the form (100 X FEV_1/FVC) = $\log_e$ (height), age, age^2, sex, sex x age, spirometer used, and place (R^2 = 0.11). Data are presented using area specific least squares (100 X FEV_1/FVC) means taken at the mean values of the covariates.

TABLE 6/2
(100 X FEV_1/FVC) MEASUREMENTS IN ADULTS BY AREA*

FEV_1/FVC by sex and by smoking status		AREA IA	 SR	 DCCI	 SR-M
Men	N	678	245	157	148
unadjusted values					
smoking: current		75.9 (0.8)	75.7 (1.1)	76.9 (1.2)	75.9 (1.2)
ex		73.6 (0.9)	74.6 (1.2)	74.2 (1.6)	74.5 (1.4)
never		78.5 (0.4)	80.2 (0.7)	77.3 (1.1)	81.2 (0.9)
Women	N	700	230	169	132
unadjusted values					
smoking: current		77.6 (0.8)	78.5 (1.5)	77.3 (1.1)	78.3 (1.6)
ex		80.5 (0.9)	79.9 (1.3)	80.6 (1.4)	81.2 (1.2)
never		81.1 (0.3)	81.4 (0.6)	78.6 (1.0)	81.4 (0.8)
Men and Women	N	1378	475	326	280
unadjusted		78.7	79.2	77.5	79.0
adjusted (external)					
smoking: current		93.2 (0.6)	93.0 (1.0)	93.8 (0.9)	93.2 (1.0)
ex		93.3 (0.8)	93.6 (1.2)	94.7 (1.3)	93.5 (1.5)
never		97.9 (0.3)	98.0 (0.5)	95.6 (0.8)	98.9 (0.7)
adjusted (internal)		78.5 (0.2)	78.5 (0.3)	77.7 (0.4)	78.7 (0.4)

---

* Men were at least 15 years of age and women at least 13 years of age. Percent predicted is as defined in previous table. For internal adjustment, the association between (FEV_1/FVC) was estimated using the equation of the form: (100 X FEV_1/FVC) = age, sex, FVC^2, sex x FVC^2, spirometer used, current number of cigarettes smoked daily, cumulative number of cigarettes smoked, and place (R^2 = .40). Data are presented using area specific least squares (100 X FEV_1/FVC) means taken at mean values of the covariates age, sex, and FVC.

TABLE 6/3

COMPARISON OF CRUDE AND ADJUSTED* DIFFERENCES IN THE PROPORTION OF SUBJECTS WITH AN FEV_1/FVC RATIO LESS THAN 70%.

% With FEV_1/FVC < 70%:	IA	SR	Difference (IA - SR) Crude	 Adjusted
Adults	14.4	12.4	2.0	1.1
(p-value)			(p=.28)	(p=.68)
Children	1.8	2.8	-1.0	-3.6
(p-value)			(p=.42)	(p=.08)

* Controlling for the potential confounding variable listed in this section.

TABLE 7/1

THE INFLUENCE OF INCREASED BRONCHODILATOR RESPONSIVENESS ON THE RELATIONSHIP BETWEEN FEV_1 AND AREA*

Age Group	Bronchodilator Response	N	AREA					
			IA (1)	SR (2)	Diff. (1-2)	DCCI (3)	SR-M (4)	Diff. (3-4)
Children		683						
	increased	68	2.05	1.94	+.11	2.01	2.02	-.01
	not increased	615	2.27	2.20	+.07	2.22	2.20	+.02
Adults		1925						
	increased	197	3.16	3.15	+.01	3.22	3.13	+.09
	not increased	1728	3.58	3.57	+.01	3.58	3.62	-.04

* Table shows internally adjusted mean FEV_1 values by age group and bronchodilator response dichotomized as increased, i.e. the top decile of response to 1 dose of terbutaline aerosol, and not increased, i.e. not in the top decile. Children aged 7-12 years old were administered 250 ug. of terbutaline and older individuals were administered 500 ug. The aerosol was administered using a 750 ml. spacer and the FEV_1 response was measured 20 minutes later.

TABLE 7/2

MEAN PERCENTAGE BRONCHODILATOR RESPONSE BY AREA*

Bronchodilator response by age group, sex, and smoking status	AREA			
	IA	SR	DCCI	SR-M
Children N	395	178	110	116
Unadjusted				
boys	1.1 (0.3)	3.1 (0.9)	1.5 (0.8)	3.0 (1.1)
girls	1.0 (0.4)	1.7 (0.6)	0.8 (0.7)	1.2 (0.8)
boys and girls	1.1 (0.3)	2.4 (0.6)	1.2 (0.6)	2.2 (0.7)
Adjusted (internal)	1.1 (0.3)	2.6 (0.5)	1.3 (0.6)	2.4 (0.6)
Adults N	1201	428	296	256
Unadjusted by smoking				
current	2.5 (0.4)	2.7 (0.5)	1.3 (0.4)	2.4 (0.4)
ex-	3.1 (0.3)	3.0 (0.5)	2.6 (0.5)	2.7 (0.6)
never	2.6 (0.2)	2.5 (0.3)	2.4 (0.5)	2.0 (0.4)
combined	2.6 (0.2)	2.6 (0.2)	2.1 (0.3)	2.2 (0.3)
Adjusted (internal)	2.6 (0.1)	2.7 (0.2)	2.1 (0.3)	2.3 (0.3)

* For children, the association between bronchodilator response and area was estimated using the equation of the form: bronchodilator response = sex, $\log_e$ (age), age^2, sex x $\log_e$ (age), sex x age^2, place ($R^2 = .03$). For adults, the association between bronchodilator response and area was estimated using the equation of the form: bronchodilator response = sex, age, age^2, $\log_e$ (age), current number of cigarettes smoked daily, place ($R^2 = .03$). Results are presented by using the area specific least squares bronchodilator response means taken at the mean values of the covariates.

TABLE 7/3

COMPARISON OF CRUDE AND ADJUSTED* DIFFERENCES IN THE PROPORTION OF SUBJECTS WITH BRONCHODILATOR RESPONSE GREATER THAN 7.7%.

			Difference (IA - SR)	
% With > 7.7	IA	SR	Crude	Adjusted
Adults	10.0	7.9	2.1	0.3
(p-values)			(p=.214)	(p=.89)
Children	5.6	14.0	-8.4	-12.4
			(p<.01)	(p<.01)

* Controlling for the potential confounding variables listed in this section.

Appendix 16.5

DEVELOPMENTAL CHARACTERISTICS OF CHILDREN
N VALUES FOR TABLES 16.5/1 AND 16.5/2

DEVELOPMENTAL CHARACTERISTICS OF CHILDREN
N VALUES FOR TABLE 16.5/1

	AREA			
	IA	SR	DCCI	SR-M
Infants with delayed development				
Boys	120	54	50	15
Girls	115	61	57	14
Total	235	115	107	29
Parents not satisfied with development				
Boys	120	54	50	15
Girls	115	61	57	14
Total	235	115	107	29

DEVELOPMENTAL CHARACTERISTICS OF CHILDREN
N VALUES FOR TABLE 16.5/2

	AREA			
	IA	SR	DCCI	SR-M
Height below 5 %ile	914	405	280	209
Weight below 5 %ile	915	404	278	209
Denver Developmental Screening Test	69	12	25	6
Delayed Sexual Maturity				
Boys	77	37	15	24
Girls	111	50	25	28

Number/
Numéro

4

Acid
Deposition
Research Program

THE SOUTHWESTERN ALBERTA MEDICAL DIAGNOSTIC REVIEW

SUMMARY

METHODS AND RESULTS

DESIGNED AND EXECUTED BY:
THE McGILL INTER-UNIVERSITY RESEARCH GROUP

PRINCIPAL INVESTIGATOR: DR. WALTER O. SPITZER, M.D., CHAIRMAN
OF EPIDEMIOLOGY AND BIOSTATISTICS,
McGILL UNIVERSITY, MONTREAL, CANADA

SUPPORTED BY A GRANT: COMMUNITY AND OCCUPATIONAL
HEALTH, GOVERNMENT OF ALBERTA

ADMINISTERED BY: ALBERTA GOVERNMENT/INDUSTRY
ACID DEPOSITION RESEARCH PROGRAM

JUNE 1986

SOUTHWEST ALBERTA MEDICAL DIAGNOSTIC REVIEW PROJECT

SUMMARY

by

McGill Interuniversity Research Group

with

the Epidemiology Rapid Response Unit
of the Montreal General Hospital

Note

1) To facilitate reference to the complete report, the numbering system used in this summary is basically the same as that used for the complete report.

2) This is a summary of the final report of the MDR. In the interests of providing the public with the report at the time of the community meetings, and because of the compressed time frames involved in report production, some typographical or arithmetical errors may exist. Further exhaustive editing is in progress.

The definitive version eliminating any such production errors will be printed by the fall of 1986.

CREDIT AND RESPONSIBILITY

The completion of this Medical Diagnostic Review in Southwestern Alberta and the preparation of this final report in one year is a tribute to the teams of men and women in the inter-university research group co-ordinated by McGill University and our colleagues associated with the Acid Deposition Research Program (ADRP).

The co-investigators and professionals listed in the next pages have earned most of the credit for the timeliness and the quality of this study. Having benefitted from the wise counsel of many senior peers and my staff the responsibility for the conclusions published and for any errors is mine alone.

This document, in two volumes and several technical appendices, has been submitted to The Honourable Mr. James F. Dinning, Minister of Community and Occupational Health and to the Co-Chairmen of the ADRP at Edmonton on June 9, 1986.

My colleagues and I thank the government and the citizens of Alberta for the trust placed in us in helping resolve with them one of the most challenging Canadian problems at the interface of the environment and the health of the public.

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Strathcona Professor of Preventive Medicine
Professor and Chairman of Epidemiology and Biostatistics
Professor of Medicine
McGill University

Principal Investigator
Southwest Alberta Medical Diagnostic Review

Montreal, June 9, 1986

Universities' Contributing Scientists and Professionals
for the
Medical Diagnostic Review
# of the
Acid Deposition Research Program
in
Alberta

McGill University (Coordination)
University of British Columbia
University of Manitoba
University of Calgary
Laval University (Laboratory)
York University
Mayo Clinic (Laboratory)
University of Toronto

The Southwest Alberta Medical Diagnostic Review Project was funded by the Department of Community and Occupational Health of Alberta and administered by the Acid Deposition Research Program.

Acid Deposition Research Program

Co-Chairmen: Mr. Ronald L. Findlay
Mr. Carl L. Primus

Program Manager: Dr. Ronald R. Wallace

Communications
Coordinator: Ms. Jean L. Andryiszyn

DEFINITIONS AND FREQUENTLY USED TERMS

ADRP - Acid Deposition Research Program.

A priori - Refers to statements or assumptions or statistical criteria set forth in advance of commencing the field work of the Medical Diagnostic Review Project (MDR); the converse of this term in the report is either post-hoc or a posteriori.

Algorithms - A step-by-step procedure for solving a problem or accomplishing some end; in the clinical context this refers to classification methods or treatment decisions done by pre-determined ground rules.

Biostatistics - Quantitative methods of analysing information about living creatures.

CAB - Community Advisory Boards.

CHS - Canada Health Survey: data is from 1978-79 Statistics Canada Health Survey and figures quoted are for all of Canada except when specified.

Cardinal clinical outcome - The symptoms, signs and diagnoses that are most plausibly associated with the environmental risk factors of concern in the Index Areas.

Clinical epidemiology - The study of determinants and effects of clinical decisions.

Clinical significance - A difference sufficiently great that it is impressive because of its consequences for the health of people; clinical significance takes into account the unavoidable reality of uncontrollable or unforeseeable biases as well as real but trivial differences; clinical significance is referred to as "delta" by many statisticians and in every day language it could be referred to as "the difference that makes a difference".

Clustering - The phenomenon of "bunching-up" of people or events or diagnoses; clustering could be in relation to time (for instance there may be an unusual number of cases of measles within a three-month period in a given location), it could be in relation to geography (there might be an unexpectedly high number of cases of absenteeism from school in one village as compared to surrounding ones); clustering could be in relation to diagnosis itself (even though total mortality due to heart disease might be the same in two areas, one could note a clustering of many cases of heart attack in one community versus another).

Cohort - A group of persons sharing common characteristics at a given point in time and defined by an event such as birth, admission to hospital or residence in a particular location.

Corroborate - In the context of this report, corroboration occurs when in comparisons of DCCI versus SR-M the direction of the difference and the magnitude of the difference observed is similar to differences noted in the comparison of IA versus SR.

DCCI - Didsbury - Carstairs - Crossfield - Irricana, exposed control area, north of Calgary.

Demography - The statistical study of human populations especially with reference to size and density, distribution and vital statistics.

Epidemiology - The study of determinants of health and disease in human populations; it includes the study of incidence, distribution and control of disease in a population.

Etiology - Cause or the study of cause.

Heavy (or trace) metals - Metals found in the environment that could penetrate a person's system to dangerous or toxic levels.

IA - Index Area, or the main area of interest exposed to environmental contaminants of concern. An area of southwestern Alberta in and around the towns of Twin Butte, Glenwood, Hill Spring, Willow Creek and Mountain View.

IA (MC) - Index Area outmigrants most comparable to outmigrants from SR and DCCI, consisting only of first degree relatives from the IA outmigrants respondents.

Incidence Period - January 1, 1970 - December 31, 1984

Incident Cancer - Any cancer occurring in a member of the Index Area 1970 cohort during the incidence period as registered by the Alberta Cancer Registry. (Please note: it is recognized under this definition that only cancers that occurred within the Province of Alberta will be registered and thus be considered as incident cancers.)

Index Area 1970 cohort - The collection of all individuals who were alive and resident in the Index Area during the calendar year 1970.

M - Abbreviation for population of Mormon religion.

MDR - Medical Diagnostic Review, being the formal name of this health study.

Methodology - The study of methods.

Period prevalence - The frequency of disease in a population within a span of time. Expressed otherwise, the prevalence of a particular health state or disease in a population of

interest during a period of time. For instance the number of diabetics in Toronto during one year, or two weeks. (This is to be contrasted with point prevalence which is the frequency of the disease at a given instant point in time).

Person Years of Risk - A measure of the population at risk of becoming diseased or dying during a defined period of time.

Post-Hoc Hypotheses - Hypotheses that were not formally put forward at the outset of a study but that are made only after looking at the data.

Power (to detect differences) - A measure of the strength that a study has to detect differences that are real.

Protocol - The plan of a scientific experiment or treatment recorded in writing before initiating the scientific work.

Reference rate - A measure of the frequency of disease or health-related events in a reference or control area.

RFP - "Request for Proposal".

SA - Southern Alberta, south of an east-west line running through Edmonton but excluding the Calgary and Edmonton census metropolican areas. (In some assessments Lethbridge and Medicine Hat are also excluded.)

SAB - Scientific Advisory board (appointed by the Acid Deposition Research Program).

SAG - Scientific Advisory Group (appointed by McGill University).

Signs - Observed phenomena in people's bodies as ascertained by professionally trained clinicians (usually physicians). Signs, like symptoms, are indicators of the possibility of disease but are generally considered to be objective findings in clinical research.

Sociodemographic - Attributes of people referring to vital information such as age and sex as well as social and cultural factors.

Spirogram - An instrument that measures the amount and rate of air exchange in the lungs.

SR - Stirling/Raymond, unexposed control area, south of Lethbridge, which is the main comparison area with IA.

SR-M - Stirling/Raymond minus Mormons, a subgroup found to be the best match for comparison to DCCI.

Standardized Incidence Ratio (SIR) - The ratio of the observed number of incident cancers divided by the number of expected cancers where the latter is obtained by applying to

the Index Area 1970 cohort, age-, sex-, and cohort-specific incidence rates derived from referent populations. (See definition of SMR for the description of a similar ratio applying to deaths.)

Standardized Mortality Ratio (SMR) - A rate which expresses the number of observed deaths in a defined area for a defined period compared to those you would expect if the rates of a reference population (such as an entire province) applied in the area concerned. For instance, if there were 75 observed deaths in a particular area during a decade and one expected 100 deaths in that same area given the provincial rates, the SMR would be 0.75. In situations where there is neither an excess nor a deficit of deaths in a given area the SMR is very close to 1.0 (unity).

Statistical significance - A statement that indicates the likelihood that differences in numbers or rates or averages observed could have arisen by chance alone.

Supplemental Incidence Period - January 1, 1985 - December 31, 1985.

Symptoms - Perceptions which people have about themselves or about their body which are indicators of possible disease. Symptoms are reports of persons as patients as they describe what they feel and are generally considered to be subjective findings.

Toxicology - A science that deals both with poisons and other substances to link their effect with health problems.

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1. INTRODUCTION

1.1 Acid Deposition Research Program: An Introduction

The potential adverse impact of acid-forming emissions is one of the most significant environmental problems to be encountered in North America in the last two decades. Apart from proven effects on the environment, considerable research is to be done regarding the potential effects that these emissions may have on the health of humans, either directly through absorption and inhalation of the emissions or indirectly through ingestion of food and water.

In Alberta, the development of sulphur-containing natural resources results in the release of acid-forming emissions (e.g. SO_x, NO_x, H_2S) and other associated compounds (e.g. metal particulates, organics). The concern that these emissions may affect the health of Alberta citizens in the Index Area has been the topic of considerable discussion over the last twenty years, particularly in relation to the development of the sour gas industry. Numerous studies and public hearings have been conducted and several reports with attendant recommendations exist to try to resolve this issue. Despite these efforts, it is still unclear whether a direct cause-effect relationship exists between exposure to these emissions and reported health complaints and what role, if any, numerous confounding variables such as lifestyle may play in this problem.

In response to the continuing concern and efforts of many indi- viduals within Government, industry and the public sectors to resolve this question, the Alberta Government and a consortium of industries created jointly the Acid Deposition Research Program (ADRP) to:

- develop a comprehensive understanding of the effects of acid-forming emissions on the environment;

- provide a scientific basis for sound long-term environmental management and regulatory control of these emissions;
- disseminate such information among members, to the public and to government bodies;
- undertake any research deemed appropriate; and
- encourage and include opportunities for public representation in the ADRP.

A Request for Proposal (RFP) to undertake health studies cites the consensus (reached at an ADRP-conducted workshop in 1983) of a 23-member international panel, representing 17 areas of medical and toxicological expertise, that a comprehensive medical diagnostic review was necessary in the Index Area to determine the nature and magnitude of long-standing health complaints which residents ascribe to emissions from sour gas plants.

On May 1, 1985 it was announced to Albertans at a public meeting that a study designated Medical Diagnostic Review would begin in the summer of 1985, with the McGill Inter-University Research Group (Figure 1.1/2) undertaking the work. The study would be funded by a grant from Alberta Community and Occupational Health and administered by the Acid Deposition Research Program.

1.2 Advisory Boards, Committees and Liaison Staff

1.2.1 Scientific Advisory Board - ADRP

The Scientific Advisory Board (SAB) of the Acid Deposition Research Program authorized the RFP which gave the broad objectives guiding the initial protocol prepared and submitted by the investigators. The SAB (Figure 1.2/1) also:

- reviewed the protocol submitted and proposed certain changes accepted by the investigators;
- gave scientific clearance to proceed with the basic design

and objectives;

- made a site visit to the field in July 1985, inspected arrangements there and approved certain modifications to the protocol to accommodate field conditions, the major one relating to additional sampling of a comparison community (see 4.2);
- reviewed and commented (peer review) on the methods report and the results and conclusions of the investigators prior to public release.

1.2.2 The McGill Scientific Advisory Group

To reduce any chance of inadvertent errors of analysis or interpretation, and to enhance the objectivity and accuracy of the Final Report, the Dean of the Faculty of Medicine of McGill University, appointed a Scientific Advisory Group (SAG) (Figure 1.2/2). This group of epidemiologists, environmental scientists, toxicologists, and clinical investigators--many with world-wide reputations--gave the data in-depth, exhaustive scrutiny before its submission to the ADRP and the Alberta Government.

1.2.3 Community Advisory Boards

A unique feature of this research project was the formal creation of three Community Advisory Boards (CAB) to complement the Scientific Advisory Board. While the SAB judged the work primarily on scientific merit the CAB had a mandate to comment and approve the relevance of the proposed work.

The CAB also helped overcome barriers to community participation; helped enhance community understanding; solved logistical problems; and helped in the identification of outmigrants. The investigators attribute the high response rates eventually attained in large measure to the CAB. (Figure 1.2/3)

1.2.4 Ethics Committee

Prior to fieldwork, an Ethics Committee was mandated by the Faculty of Medicine of McGill University to review all implications of ethical relevance. Members of the committee included scientific experts, lay persons from the Montreal area, a prominent citizen of Southern Alberta who had the confidence of the population to be studied, and representatives of the Alberta Government and the ADRP. The guidelines used were those of the Medical Research Council of Canada. The guidelines protect the anonymity of the reviewers.

1.2.5 Professional Counsel and Coordination in Communication

Coordination of communications was done by Ms. Jean Andryiszyn of the Calgary firm of Francis, Williams and Johnson Ltd., who also served as Communications Coordinator of the ADRP. The assistance and professional advice resulted in a very satisfactory relationship of mutual support between the investigators and the media, and a constant flow of information to the public.

The success in communications for the project was another important factor in attaining high response rates in all areas.

1.2.6 Support Staff of the Acid Deposition Research Program

In the phase of formulation of the Request for Proposal, Dr. Robert Rogers served as Coordinator and shepherded the application and approval process through to the time when the field work began in Alberta in early June.

From early June through the conclusion of the project Dr. Ronald Wallace functioned as Program Manager, and he made enormous contributions to assure that all operational objectives were attained.

There was no interference in the scientific conduct of the study from the ADRP staff, the administrative and physical intermediaries, or the Government of Alberta, which indirectly and ultimately funded the study.

Figure 1/1

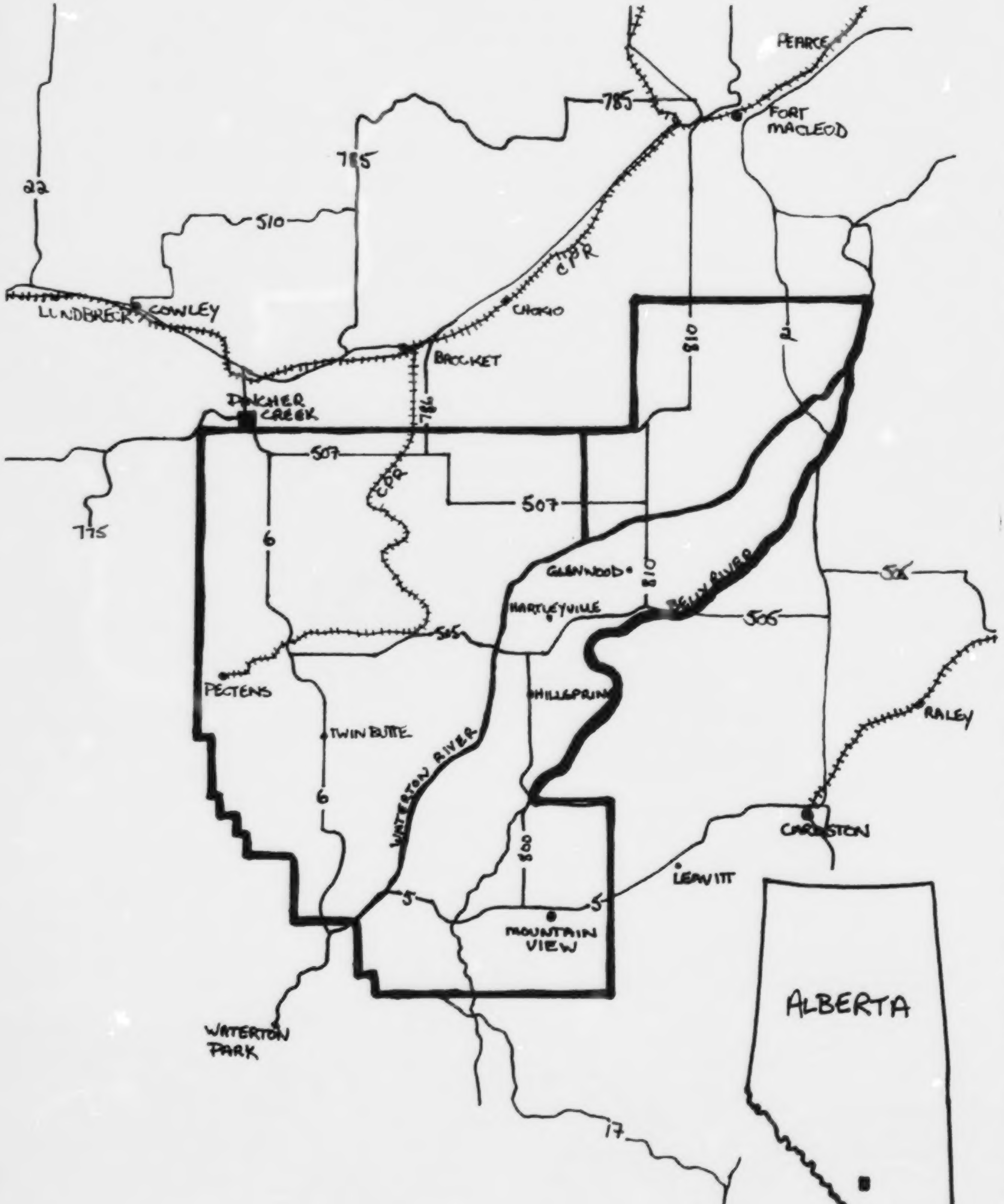
PEARCE
785
FORT MACLEOD
785
22
510
CPR
LUNDBRECK
COWLEY
CHOKIO
BROCKET
PINCHER CREEK
786
810
2
507
CPR
507
775
6
GLENWOOD
810
HARTLEYVILLE
BELLY RIVER
505
505
505
PECTENS
TWIN BUTTE
HILLSPRING
RALEY
WATERTON RIVER
6
800
CARDSTON
LEAVITT
5
5
MOUNTAIN VIEW
WATERTON PARK
17
ALBERTA

Figure 1.1/2

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Editorial Coordinators:
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Figure 1.2/1

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Figure 1.2/2

SCIENTIFIC ADVISORY GROUP MEMBERS

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Professor of Medicine
Professor of Physiology
Department of Physiology
University of Oregon Medical
School

Figure 1.2/3

COMMUNITY ADVISORY BOARD

INDEX AREA	REPRESENTING
Mrs. Sophie Taylor Pincher Creek	(Twin Butte)
Mr. Tom Ferguson Pincher Creek	(Twin Butte)
Mr. Jack Ady Hill Spring	(Hill Spring)
Mrs. Margaret Caldwell Hill Spring	(Hill Spring)
Mr. Noel Pilling Mountain View	(Mountain View)
Mrs. Laura West Mountain View	(Mountain View)
Mr. Wayne Smith Glenwood	(Glenwood)
Mr. Rudy Kutsch Glenwood	(Glenwood)
Mrs. Ellen Chester Fort Macleod	(Willow Creek)
Mr. Arthur Mathes Pincher Creek	(Industry Rep.)

Figure 1.2/3 Community Advisory Board -- continued

DIDSBURY, CARSTAIRS, CROSSFIELD, IRRICANA (DCCI)

Jessie Alcorn
Councilor
Carstairs

David Derksen
Deputy Reeve
Carstairs

Louise Feltham, M.D.
Councilor
Rocky View

Lorne Kosack
Deputy Mayor
Crossfield

David Lord
Mayor
Irricana

Brian Popp
Hospital Administrator
Didsbury

Wayne M. Ryder
Town Manager
Crossfield

Ron Stoutenberg
Administrator
Irricana

Don Watt
Mayor
Didsbury

STIRLING/RAYMOND

Marvin Dahl
Councilor
County of Warner

Dennis Fromm
Councilor
Raymond

John Maloney
Stirling Senior Citizens

Ken Moore
Mayor
Stirling

Terry Bland
Chairman
Positive Response Committee
Stirling

Don Nilsson
Councilor, Stirling

Dick Papworth
Reeve County of
Lethbridge

Arlene Sillito
Stirling Village
Office

Brad Watson
Town Office
Raymond

2. PURPOSE

The original protocol set forth the following objectives. After field work was underway and feasibility checks had been completed some modifications were made with approval of the SAB.

2.1 General Objectives at the Outset

The purpose of the Medical Diagnostic Review Project was to determine whether the residents of the Index Area experience adverse health effects more often than is expected from frequencies derived or observed:

1) In two carefully selected control areas within Alberta, one that is demographically similar to the Index Area in all respects, but not exposed to sour gas refineries and one that is representative of Southern non-metropolitan Albertans exposed to sour gas;
2) In the general population of Alberta; and
3) In subsets of the entire Canadian population where either similarities or contrasts could be illuminating.

Figure 2.1/1 shows the Index Area and the control areas within Alberta which were eventually selected as reference populations. See Chapter 4 for the methods employed to select the reference areas.

2.2 Specific Research Objectives Set Forth in the Protocol

These were the specific research objectives of the study:

1) Determine the frequency of health problems and diagnoses among residents of the Index Area that are alleged to be associated with the type of industrial pollution found in the vicinity.
2) Determine, for comparison, when feasible, the frequency of similar health problems in (i) Alberta as a whole, (ii) selected rural areas of Alberta that are geographically and demographically similar, (iii) other rural areas in Canada that are demographically similar

and (iv) other areas from anywhere in Canada where data gathering tactics very similar to those employed by the Canada Health Survey had been used. The reference areas that proved to be feasible are the population in Toronto from the Junction Triangle study, Southern Alberta, and Canada using Canada Health Survey data (see definitions).

3) Determine, empirically, the current frequency of health problems and diagnoses of the type alleged to be associated with exposure to the emissions of the sour gas industry in the Index Area and two comparable areas of Alberta. One of these "control" or reference areas is sociodemographically very similar to the Index Area and not exposed to the sour gas industry. The other is sociodemographically representative of southern rural Albertans as a whole, but is exposed to sour gas emissions.

4) Determine whether the current frequencies of these health problems and diagnoses for the Index Area differ in any way from those in the two areas selected as controls.

5) Determine whether the incidence of and mortality from cancer differ, in any way, from those in census tracts elsewhere in Alberta chosen for their sociodemographic similarity and whether they differ in any way from the cancer incidence experience of Alberta as a whole.

6) Determine whether the frequency of ascertainable reproductive abnormalities and birth defects differ from that observed in demographically similar areas elsewhere in Alberta, in the province as a whole and in any well-defined Canadian jurisdiction for which good quality numerator and denominator data can be obtained.

7) Determine the frequency of disability and debility days experienced by the study population in the Index Area and the control areas, and then compare it with rates derived in the Canada Health Survey for the Prairies and Canada.

8) Evaluate the severity of adverse health outcomes, if any, observed in the Index Area, and describe their clinical, social, and economic significance mainly through comparison with the control areas.

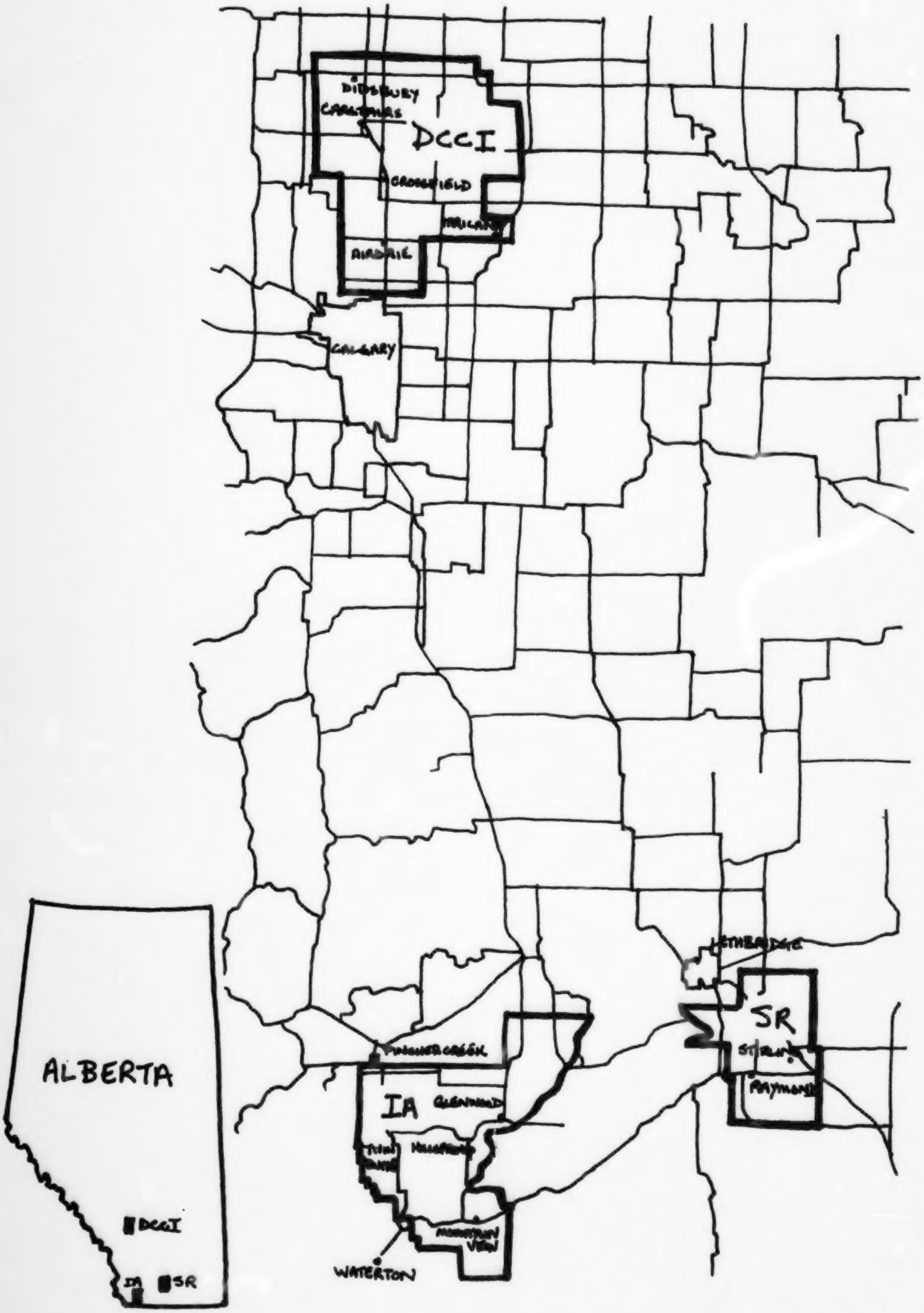
9) Determine, through clinical and laboratory strategies the extent of any evidence of contamination of Index Area residents with selected heavy metals and other substances alleged or shown to be noxious to health.

10) Determine average annual mortality in the Index Area and compare it to the rates in the control areas and primarily with that of Alberta as a whole.

11) Determine whether there is any temporal, geographic or clinical clustering of any adverse health phenomenon that might provide insight into the possible effects of relevant exposures.

12) Report all of the findings in a manner that is both uncompromising with regard to their scientific and analytic admissibility, as judged by peer reviewers, and understandable to the general public, governmental policy makers and health providers who will use the data as the basis for public health policy affecting citizens similarly exposed.

Figure 2.1/1


DIDSBURY
CARSTAIRS
DCCI
CROSSFIELD
IRRICANA
AIRDRIE
CALGARY
LETHBRIDGE
SR
STIRLING
RAYMOND
PINCHER CREEK
IA
GLENWOOD
TWIN BUTTE
HILLSPRING
MOUNTAIN VIEW
WATERTON
ALBERTA
DCCI
IA
SR

3. ADMINISTRATION OF THE MDR PROJECT AND LOGISTIC ACCOMPLISHMENTS

3.1 Introduction

Since this was probably one of the largest clinical epidemiology field studies ever conducted in Canada, there was no model or precedent to follow. The greatest asset was the highly-committed team of advisors, investigators and research staff (more than 100 individuals) that agreed to undertake this project on very short notice. Staff recruiting and training also were obviously critical to the project.

The results of the collaborative effort was the successful completion of all summer field work in Alberta following a June start, one week earlier than originally anticipated with all response rate goals attained.

For the Index Area, eleven ATCO trailers were set up in Hill Spring (Figure 3.1/1) to accommodate the clinical facilities. In the control areas, the Crossfield Curling Club and a number of ATCO trailers were used, while in Stirling, the local school was used. Transportation, meals and lodging were arranged for a team of 11 who returned in January, 1986 for the Winter Reassessment. Clinical facilities included the Glenwood Church of the Latter Day Saints and the Stirling Senior Citizens' Centre.

3.2 Summary of Chronology of Major Events of the Project

3.2.1 Planning

December 1984	"Request for Proposal" released by the ADRP.
February 10, 1985	Submission for proposal sent to the ADRP senior members.

March 1985	Meeting in Atlanta with the Scientific Advisory Board, the main investigators and the ADRP.
April, 1985	Agreement in principle reached in Edmonton. Recruiting of physicians begins, trip to Alberta to arrange for trailer rentals and accommodations. Site Manager arrived to make contacts and set up the site.
May 1, 1985	Official announcement of the project made in Pincher Creek, Alberta by the Minister and Deputy Minister of Social Services and Community Health and the Program Manager from the ADRP. (The funding department is now known as Community and Occupational Health.)
May 3, 1985	First meeting with the Index Area Community Advisory Board.
May 1985	Development of questionnaires and data-gathering instruments. Final accommodation arrangements made. Hiring of support staff, interviewers and coders. Training of interviewers and coders.

3.2.2. Field Activities

May 28, 1985	Five senior personnel arrive in Alberta.
May 31, 1985	Thirty staff members arrive in Alberta.
June 1985	Enumeration of Index Area.
June 1-2, 1985	Initial training of ritualistic physicians.
June 4-5, 1985	Set up of clinical supplies, coding area and computers.
June 6, 1985	Saw first participant.
June 28, 1985	Arrival of the remaining staff.
July 4, 1985	Seeing approximately 60 participants per day.
July 8, 1985	Seeing 70-80 participants per day.

July 1985	Arrangements made for sites in two control areas.
July 24, 1985	First participants seen in the Stirling control areas.
July 28, 1985	On-site inspection of clinical facilities and laboratories by the SAB.
August 3, 1985	Successful completion of field work in the Index Area.
August 5, 1985	Beginning of outmigrant enumeration.
August 8, 1985	First participants seen in the Crossfield control area.
August 24, 1985	Successful completion of field work in both control areas.
September 6, 1985	Completion of data entry and community verification of the outmigrant list of all three areas.

3.2.3 Data Verification, Analysis and Production of the Final Report

October 1985	Opening of office in Calgary to process outmigrant returns and contact outmigrants to encourage their response.
October 15, 1985	Outmigrant questionnaire mailout begins continuing on an ongoing basis as new information became available.
Dec. 30-31, 1985	Second mailing to all outmigrants who had not yet responded to the questionnaire.
Jan. 22-30, 1986	Winter Reassessment exercise.
May 1986	Report complete. Review by the McGill Scientific Advisory Group, followed by the ADRP Scientific Advisory Board.

3.2.4 The Final Report: Presentation and Follow-Up

June 11, 1986	The public meeting at Pincher Creek is held to release the report publicly to the Community Advisory Boards, the scientific peers in Alberta, to the general public and the media.

June 12-15, 1986	The Co-Principal Investigators interact with small groups of the communities in the Index Area to answer questions and interpret results.
June 19, 1986	Under the auspices of the Summer Epidemiology Studies Programme of the Faculty of Medicine of McGill University, an invitational scientific meeting is held to present the findings to the scientific community in Eastern Canada, Northeastern U.S.A., and selected scientists from other parts of North America.

Figure 3.1/1

4. DESIGN OF STUDY

4.1 General Plan

4.1.1 Cross-Sectional Survey

The major thrust of the Medical Diagnostic Review was a cross-sectional survey that compared the health status of all eligible residents in the Index Area with that of samples drawn from two comparable areas of Alberta. The cross-sectional survey assesses those who lived in the Index Area (IA) in 1985 and compares them with those who lived in the comparable areas.

One comparison area in Alberta was chosen to be as free as possible from any exposure to industrial or man-made contaminants of the environment and sociodemographically comparable to the Index Area. This control area was Stirling/Raymond (SR). The McGill Inter-University Research Group declared in advance that the principal contrast is between the IA and the SR areas for health status as of 1985 evaluations.

The other control area was not sociodemographically comparable to the Index Area but was representative of the sociodemographic characteristics of non-metropolitan Southern Albertans and was exposed to emissions of sour gas. This control area was Didsbury-Carstairs-Crossfield-Irricana (DCCI).

The health indicators of citizens of the three areas were assessed in exactly the same way and at the same time of the year (summer 1985). A subsample of respondents was reassessed during the winter of 1986 to establish whether there had been any inter-seasonal variation in respiratory signs and symptoms, skin abnormalities, manifestations of allergy and pulmonary function.

4.1.1.1 Target Variables

The target variables (or key dependent variables) specified in the protocol of the MDR were these:

- Mortality;
- Frequency of serious irreversible chronic disease;
- Incidence of cancer;
- Prevalence and incidence of reproductive outcomes and birth defects;
- Levels of trace metals in the population;
- Pulmonary function; and
- Health status including:
    - burden of symptoms;
    - burden of signs; and
    - laboratory profiles.

The foregoing are single or composite variables. Summary expressions have been derived for most composite variables incorporating groups of assessments.

4.1.2 Cohort Comparison Study

A cohort analytic or cohort comparison study was also conducted. A cohort is a "closed" assembly of persons sharing common characteristics at a given point in time defined by an event (such as birth). In this study, there are two important dates that affect the strategy of following people over time (also known as a longitudinal follow-up). One is 1957, just before the first exposure to emissions from sour gas plants occurred in the Index Area. The most important inception point is 1970, for two reasons:

1) Sufficient time had passed in 1970 so that delayed adverse health effects which take time to become apparent had a reasonable chance to have become manifest;

2) The span of time between 1970 and 1985 provides sufficient years of follow-up to identify adverse health events of importance such as new cancers occurring since 1970, or of detectable diseases in the respiratory or neurological systems.

Thus for purposes of a cohort strategy to study health problems in Southern Alberta, the most important denominator of people delineated is the 1970 cohort of residents defined as living in the Index Area at the time. The 1970 cohort was followed forward in time through August 1985. Samples of the 1970 cohort of the SR and DCCI areas were also studied.

The most important purpose of conducting a longitudinal follow-up of persons who were in the Index and Control Areas as of 1970 is to determine whether there had been selective unequal health-related migration in the Index Area compared to the main comparison areas (SR). For example, this follow-up would provide a check on questions such as: had all sicker people left the Index Area (or indeed died); or conversely, had the healthier more energetic ones moved out of the area.

Another cohort was that identified for the cancer component of the study and related to the experience of all of Alberta and selected areas of Sourthern Alberta alone.

4.2 Selection of Comparison Areas

Initially, the protocol had specified the use of two control areas both as sociodemographically comparable to the Index Area as possible. One of the control areas would not be exposed to sour gas emissions, while the other would be exposed.

However, the geography and demography consultants soon determined that while there was a very comparable non-exposed community, there were no exposed areas in Southern Alberta which are sufficiently demographically comparable to the Index Area to be properly considered an Exposed Most Comparable Area for reference purposes.

Accordingly, the strategy was altered with SAB approval to have an Exposed "Representative" Control Area. This control area is the most comparable to the Index Area with respect to exposure and it is also highly representative of the "Average Non-Metropolitan Southern Albertan".

Evaluation of demographic similarity was based on twelve variables selected from the 1981 Census of Canada. These represented a wide range of demographic characteristics including age structure, family size, mobility, income, educational achievement, occupational status and religion. Because of the relatively large Mormon population in the Index Area, religion was deemed to be a particularly important variable for comparison with other parts of Alberta.

Overall, the Index Area compared to other areas of Alberta has a considerably younger population, a much larger family size, a higher proportion of persons with university training, a much higher proportion of agricultural workers and a less mobile population. It enjoys about the same income as the average tract and has an average proportion of persons with low educational achievement.

In terms of religion, it is dramatically different from the average with much lower proportions of United Church adherents and Catholics and a very high proportion of Mormons.

It should also be noted that the Index Area is not homogeneous. A number of contrasts were noted especially concerning religion and economic status depending on location within the area.

The indicator of similarity among two or more communities or populations is expressed in a social distance score, with 0 denoting perfect similarity. Social distance scores for reference populations under 10 are workable, while scores higher than 20 render the communities impossible to compare even with statistical adjustments. The SR area has a social distance similarity score of 1.4 when compared to IA. As noted earlier, no similar exposed community could be found.

In general, the SR area, with the exclusion of Raymond is slightly lower on younger children and university educated, but otherwise similar demographically; not exposed to any known source of industrial pollution; relatively compact spatially; and within commuting distance of the Index Area.

Meanwhile, the DCCI area chosen, while it has a much higher proportion of non-Mormon religion, dramatically smaller family and fewer children and slightly more affluent than those in the Index Area, is representative of non-metropolitan Southern Alberta, and is also exposed. By excluding the Mormons of the SR area (SR-M), a control group characterized as "Unexposed Average Non-Metropolitan Southern Albertans" became available for reference purposes.

4.3 Outmigrant Identification for Bias Assessment

As explained earlier under section 4.1, positive identification of outmigrants and documentation of their health is essential to determine whether there was biased selective outmigration due to health reasons among the three areas. Also, outmigrant identification is essential for the cancer and the reproductive cohort studies.

The information collected among outmigrants includes:

1) readily diagnosed irreversible disease;
2) readily diagnosed serious disease, whether reversible or not;
3) reproductive outcomes and birth defects;
4) death, general and disease-specific (all cancers, all respiratory-linked).

Other data collected include demographic characteristics, residence information in the study area, and reasons for moving. The information was obtained through mail-in questionnaires, the data collection procedures being the same for each area.

In the Index Area, as close as possible to the total list of outmigrants was reconstructed, particularly because of the requirements for the cancer study. In the control areas, the outmigrant ascertainment was limited to the immediate relatives of the study participants (children, siblings and spouse's siblings). For comparisons across the three outmigrant populations, the same sampling criteria and methods were used to select a reconstructed subsample of outmigrants from the complete Index Area outmigrant list.

The task of identifying all otmigrants in the Index Area was monumental and included manual searches of municipal tax records; completion of outmigrant information forms, review of summary packages by study participants and a phone survey of study participants, continued consultation with the Community Advisory Board and knowledgeable citizens, searches of school and church records, review and links with Alberta vital statistics sources, newspaper ads asking for outmigrant information, and edit after edit of the list to eliminate duplications, spelling errors, and inconsistencies.

It is important to emphasize that a key criterion which determined eligibility of a candidate to be confirmed as an outmigrant required that there be two independent sources giving evidence of the existence of the outmigrant and the fact that he or she lived in one of the three areas in 1970.

Subsequent to mailing out of questionnaires to outmigrants, follow-up strategies to maximize response rates included one or more telephone calls and subsequent mailouts.

5. HEALTH STATUS EVALUATION

5.1 Cross-Sectional Survey

5.1.1 Selection of Subjects, and Sampling

A complete census of all residents of the Index Area was taken, and all these persons were eligible study subjects.

In the SR area the sample of individuals representative of this comparison area was selected in two stages. Firstly, a complete census of all residents was done. Secondly, in order to obtain the required sample size of 900, with one-third or more being Mormons, a stratified probability random sample was drawn.

The slection of the sample from the very large and more populous DCCI area was made in three stages: a census of all households, an enumeration of a random sample of households, and a stratified random sample of individuals (excluding Mormons) from the randomly enumerated households.

5.1.2 Data Gathering Procedures

Data for the cross-sectional survey were obtained by means of an interviewer-administered questionnaire, a "ritualistic" medical examination, a laboratory profile, a "judgemental" medical examination by prescriptive and discretionary use of ultra-specialized tertiary medical consultation.

The Questionnaire

The categories of information elicited with the questionnaire are:

1) demographic characteristics;
2) risk factors;

3) life style;

4) self-reported symptoms and illnesses;

5) health service utilization;

6) disability; and

7) reproductive history.

The sections dealing with chronic illness, use of medical services and disability were identical to those used in the Canada Health Survey whenever possible, while sections dealing with respiratory illness were identical with those used and validated by the American Thoracic Society 1978 Respiratory Symptoms Questionnaire. This was done to facilitate any illuminating comparisons with other national and international data sets.

Three age-specific childhood questionnaires were used, which were answered by one parent then linked to that parent for common demographic risk factors and lifestyle information.

The Ritualistic Medical Examination

The ritualistic medical examination was carried out by a physician specifically trained to carry out this type of research-oriented examination. The physicians examined the patient following a rigidly prescribed protocol consisting of 74 specific items for adults. To reduce observer variation, all findings were recorded without taking a history or enquiry about the person's health in any way.

Laboratory Data

Measurements were made of height, weight and visual acuity. Electrocardiograms and spirograms were performed. Urine analyses were done. Lastly, samples of serum for biochemistry and of hair and whole blood for trace metal analysis were obtained.

The Judgemental Medical Examination

After the questionnaire, the ritualistic medical examination, and the laboratory sequence, participants went to the judgemental medical examination. This was carried out by a senior physician who had access to all the data gathered up to that point. The physician verified elements in the questionnaire, the ritualistic medical examination, and the laboratory data, and then recorded his or her conclusions on a separate form. Whenever possible, a definitive diagnosis was established and recorded. In cases of doubt or when a participant specifically requested, tertiary specialist consultation was arranged at Foothills Hospital, University of Calgary and the result subsequently entered into the data set.

5.1.3 Clinical Outcome Variables

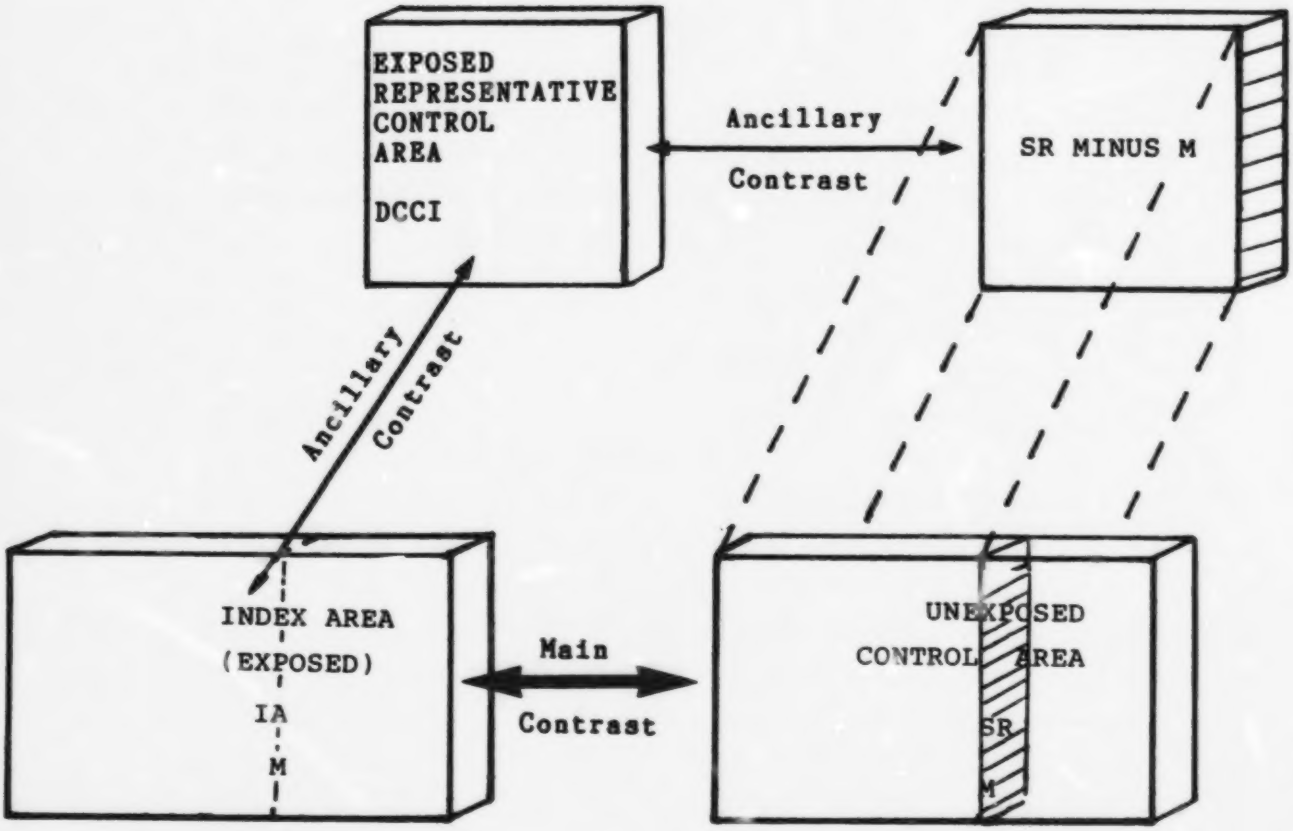
Symptoms, signs and diseases with plausible or known associations with exposure to known environmental irritants in that community were determined a priori to be the primary or cardinal clinical outcome variables. Of all the clinical data gathered during the study, those related to cardinal clinical findings were given primary importance. Other clinical findings were given less importance.

5.1.4 Contrasts of the Study

The main purpose of the study is to determine whether there was an "epidemic" of adverse health experience among residents of the Index Area. To that end, the main contrast for the cross-sectional survey of the study is to determine whether, yes or no, an epidemic has affected Index Area residents. That contrast declared a priori is the principal one for statistical considerations between the Index Area (IA) and the Stirling/Raymond area (SR) (see Figure 5.1/1).

FIGURE 5.1/1

PLANNED CONTRAST FOR CROSSECTIONAL SURVEY


EXPOSED
REPRESENTATIVE
CONTROL
AREA
DCCI
Ancillary
Contrast
SR MINUS M
Ancillary
Contrast
INDEX AREA
(EXPOSED)
IA
M
Main
Contrast
UNEXPOSED
CONTROL AREA
SR
M

M = Population of Mormon religion

FIGURE 5.1/1 (continued)

PLANNED CONTRAST FOR CROSSECTIONAL SURVEY

Note: IA and SR are very similar sociodemographically. DCCI and SR-M (Mormons excluded) are very comparable sociodemographically. DCCI very similar to all 119 provincial census tracts south of Edmonton (considered together) excluding Edmonton and Calgary.

Main Contrast: IA compared to SR

- to establish whether there is an "epidemic" of compromised health among residents of the Index Area IA;
- settles main questions of study as set forth in advance.

Ancillary Contrast:

IA compared to DCCI

- in the event of differences found between IA and SR, verifies whether there are consistent patterns of change that could point to exposure as a plausible candidate for causal significance.

DCCI compared to SR-M

- in the event of differences found between IA and SR, if the same direction and magnitude is observed between DCCI and SR-M then the validity of findings for the main contrast (IA vs. SR) is buttressed;
- the contrast of DCCI vs. SR-M sheds some light on the possible effect of sour gas emmissions on representative non-metropolitan Albertans since both populations are highly similar to each other and each in turn to the entire rural population of southern Alberta.

A first ancillary contrast is between IA and the exposed representative control area in DCCI. Should there be differences between IA and SR, most particularly should IA be in worst health than SR according to our indicators, the comparison with DCCI, which is also exposed, should give valuable clues about the likelihood that sour gas emissions are responsible for such adverse effects. If the residents of the DCCI area have adverse profiles compared to SR, and similar to the IA profiles, the evidence starts to be much more solid than it would have been with only one comparison.

By removing Mormons from the SR sample, the result is what was designated the SR-M group. This group is not only very similar to the DCCI, but both are very similar to southern non-metropolitan Albertans in general. Thus, a second ancillary comparison, DCCI contrasted to SR-M, would further buttress the validity of any findings in the main contrast, particularly if they are of the same direction and of the same order of magnitude.

Moreover, although the interpretation would have to be guarded and cautious, the contrast of DCCI with SR-M would shed some light on the possible effects of sour gas emmissions on representative non-metropolitan Albertans since both populations are highly similar to each other and each in turn to the entire rural population of Southern Alberta.

Should all contrasts, the main contrast and the two ancillary contrasts show no statistical and clinical differences in any direction, this would be very strong evidence suggesting that there have been no adverse health consequences to the residents of the Index Area and to the representative area of rural Albertans in general.

5.2 Cohort Analytic Historical Follow-Up

As explained in Chapter 4, the cohort or longitudinal follow-up is important to eliminate the possible contribution of any differential health related selective migration. Aside from the outcomes related to the cancer and reproductive studies, other important outcomes like diagnosis of serious diseases could be compared between the three study areas. These outcomes were measured the same way in all outmigrants. The cohorts were formed as follows:

Index Cohort - includes all the participants seen in the summer of 1985 who were also living in the area in 1970. Added to the group are the outmigrants identified as living in the area in 1970, and those residents who have died since 1970.

Control Area Cohorts - include all the participants in each area seen in the summer of 1985 who were also living in the area in 1970. Added to the group are the outmigrants identified by the 1985 participants to be close relatives and living in the area in 1970, as well as those residents of the area who have died since 1970.

In addition to the basic information on gender, date of entry and exit from the area, date of birth, cancer and reproductive outcomes, the questionnaire asked about the time of onset and the occurrence of the following diseases: heart disease, hypertension (high blood pressure), migraine headaches, epilepsy, arthritis, chronic bronchitis or phlegm lasting more than a year, emphysema and diabetes. Data on cause of death was also obtained.

5.3 Statistical Analytical Methods

Statistical aspects of the study include discussions on measures of effect, clinical and statistical significance, effect of sample size, potential confounding variables, and quantification of key outcome variables. In advance, the magnitude of difference required for clinical significance of self-reported dichotomous attributes to be attained was specified as 10% in absolute terms when frequency of the main control was less than 10% and 20% otherwise.

Three statistical issues deserve emphasis:

1) Very large groups were under comparison and for the main contrast, IA vs. SR, there was no sampling in the IA and over 80% of the SR population was eligible to be a study subject. Expressed otherwise, the investigators studied a census or a total population in the IA empirically and a near census in the SR. This means that the usual statistical tests of inference related to sampling variation are largely irrelevant. With such large groups, most differences observed are real differences statistically speaking.

2) It is very important to consider how big the differences are biologically rather than statistically. For instance, with this sample size a difference of 3 mm. in diastolic blood pressure would have been statistically significant but biologically trivial. The investigators carefully assessed the statistical significance in all contrasts but gave much more weight to the biological or clinical importance of the differences when interpreting the findings.

3) The levels of clinical significance specified were fixed taking into account the investigators' experience with similar surveys of health population done in the past in Canada by them and also the Canada Health Survey. Clinical significance was the difference that makes a difference. Statisticians refer to such differences as "delta". For levels of clinical significance prespecified, such as 10%, the investigators are saying that anything in excess of that could not be explained either by biological variability, selective recall of respondents, observer variance or bias by measuring physicians or interviewers, and other biases.

4) For the most part, statistical significance was specified as differences greater than those that might have arisen by chance alone at the 1% level. This low 1% level was chosen conservatively because many contrasts and comparisons were being done at the same time, thus increasing the likelihood that any one of the contrasts could attain "significance" by chance alone.

6. STUDY OF CANCER RISKS AND OUTCOMES AS A COMPONENT OF THE MDR

6.1 Study Design of the Cancer Component

6.1.1 Description

The cancer component of the study was undertaken because of the perception on the part of the residents of the Index Area that the occurrence of cancer among residents of this area has been higher than they expected.

6.1.2 Objectives

The major objective of this component was to determine whether the incidence of overall cancer (as registered by the Alberta Cancer Registry) during the period January 1, 1970 to December 31, 1984 among all individuals who were alive and resident in the Index Area anytime in 1970, was higher than that which should be expected in sociodemographically similar populations in Southern Alberta during the same period.

To meet secondary objectives, because of significant local concerns with respect to differences in the cancer experience among the various communities comprising the Index Area (i.e. Mountain View, Hill Spring, Glenwood, Willow Creek and the Pincher Creek region which includes Twin Butte), the community specific cancer point prevalence for the Index Area health survey participants was to be compared.

It should be clearly stated that it was not an objective of this study to demonstrate a causal association between exposure to sour gas emissions and cancer.

6.1.3 Cohort Definition and Enumeration

This cohort was defined to include anyone who resided in the Index Area any time between January 1, 1970 and December 31, 1970 (Figure 6.1/1). Use of this closed cohort was felt to yield the optimal combination of reasonable exposure durations, plausible latency periods, sufficient subsequent observation time, increased accuracy of recall concerning outmigrants together with maximal availability and reliability of local and provincial registry information.

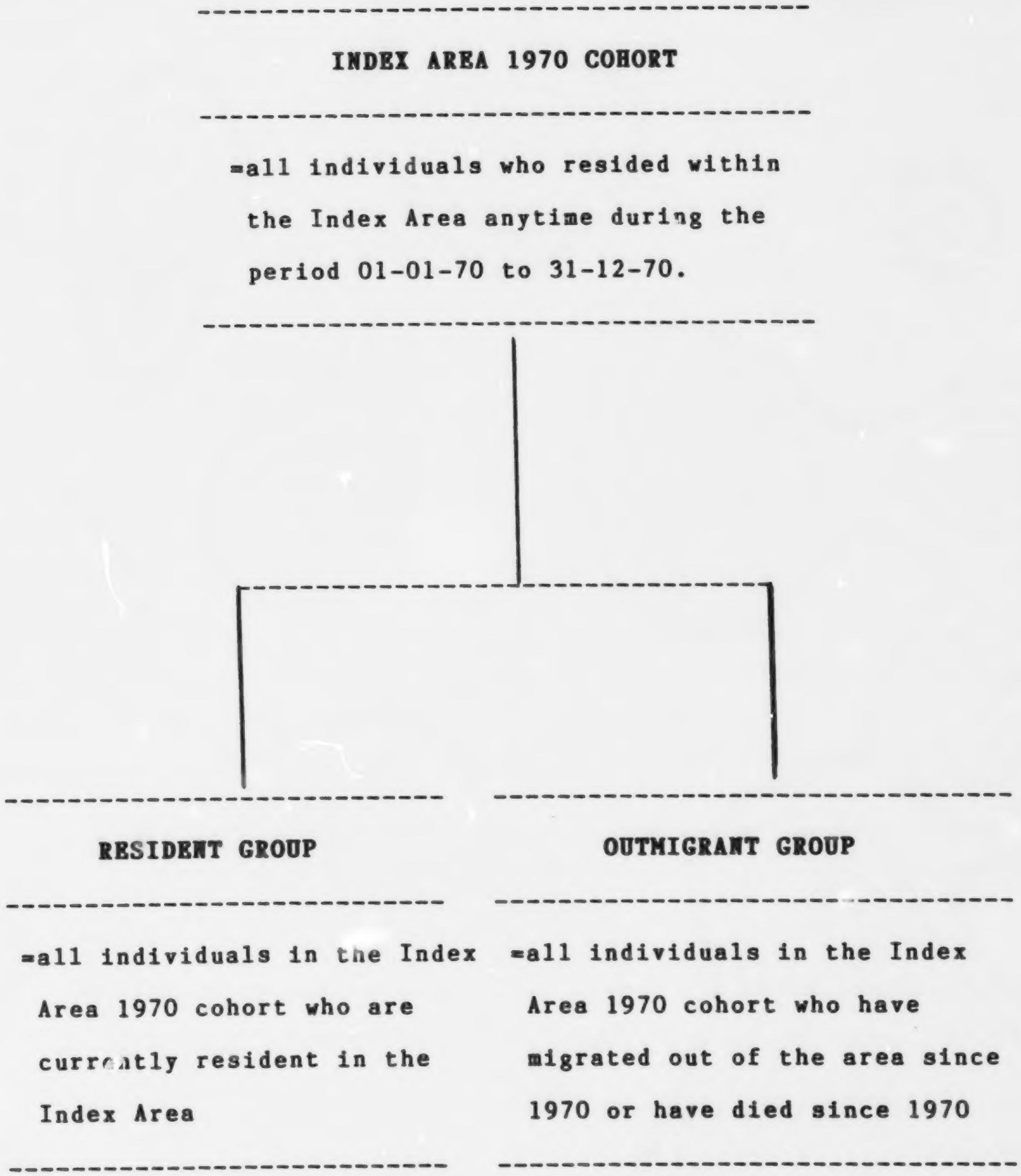
Two subgroups of the cohort were defined: the Resident Group consisting of all members of the Index Area 1970 cohort who are still residents of the Index Area; and the Outmigrant Group, those who have moved from the area since 1970 or who have since died.

The incidence period of 1970 to 1984 offers several similar advantages including plausible latency periods, reliability of registry information, and the fact that the incidence period encompasses exactly three five-year periods and that national census information is available for each such period for further comparison purposes.

It was acknowledged at the outset that the formal Incidence Period would not include cancers diagnosed in 1985. Not only is there a considerable lag time before confirmed cancers are recorded by the Alberta Cancer Registry, but the extensive health examinations conducted in the summer of 1985 were anticipated to lead to the early diagnosis of some cancers. It was expected *a priori* to have the potential to artificially inflate the cancer incidence. For these reasons the 1985 period was investigated separately with distinctive methods.

As for enumeration for this cancer component, through the questionnaire process in the Index Area it was possible to Figure

Figure 6.1/1



INDEX AREA 1970 COHORT

=all individuals who resided within the Index Area anytime during the period 01-01-70 to 31-12-70.

RESIDENT GROUP

=all individuals in the Index Area 1970 cohort who are currently resident in the Index Area

OUTMIGRANT GROUP

=all individuals in the Index Area 1970 cohort who have migrated out of the area since 1970 or have died since 1970 determine whether the resident participating in the study was a member of the Index Area 1970 cohort. It should be noted that only individuals who participated in the health survey (93% of the current residents) were eligible for inclusion in the Resident Group (RG).

The Outmigrant Group (OG) was enumerated, as described in section 4.

6.1.4 Enumeration of Incident Cancers

Three sources were used in the enumeration of incident cancers:

1) Pincher Creek Municipal District Informant List of Serious Illness, compiled by concerned local individuals;

2) the health Survey Cancer Reports compiled by the investigators as a result of questions to study participants;

3) the Alberta Cancer Registry.

Note that the first two sources served only as adjunct sources, with the Cancer Registry being the definitive source.

6.1.5 Reference Populations

Referent Population 1 = All Southern Alberta excluding the
(RP 1) metropolitan areas of Calgary,
Lethbridge, and Medicine Hat.

Referent Population 2 = Census Division 6 excluding Calgary.
(RP 2) (includes DCCI area).

Referent Population 3 = Census Division 2 excluding
(RP 3) Lethbridge.
(includes SR area).

6.2 Statistical Analysis of the Cancer Component

6.2.1 Standardized Incidence Ratios

Incident cancers, which were defined to be those occurring in the Index Area 1970 cohort and diagnosed anywhere within Alberta during the years 1970-1984, were enumerated via linkage with the Alberta Cancer Registry as described earlier. Expected rates were derived for the three sociodemographically similar referent populations.

Standardized incidence ratios were generated, being the ratio of the observed number of incident cancers divided by the number of expected cancers where the latter is obtained by applying to the Index Area 1970 cohort, age, sex, and cohort-specific incidence rates derived from referent populations.

6.2.2 Effect of Sample Size

Sample size calculations were carried out prior to the study and were based on a prior estimate of 2,000 people in the Index Area 1970 cohort with an incidence period spanning 15 years. This results in 30,000 person-years of observation forecasted. The 1978 crude all cancer incidence rate based on general Alberta population data is 3.4 cancers per 1,000 person-years of observation. (Cancer Registration in Alberta, 1978, Alberta Cancer Board). Based on this, it was expected that approximately 102 incident cancers would be observed which would yield greater than 90% power to detect small elevations in risk, that is, relative risks in the order of 1.5. By using a one-sided test with alpha = 0.05, the power to detect risks as small as 1.25 is approximately 70%. If non-melanotic skin cancer and cervical carcinoma in-situ are ignored, the 1978 Alberta crude incidence rate is roughly 2.5 per 1,000 person-years (which would yield about 75 incident cancers assuming 30,000 person-years of observation).

7. STUDY OF REPRODUCTIVE RISKS AND OUTCOMES

7.1 Study Design

In general the objective of this component of the study was to determine whether the frequency of reproductive abnormalities and birth defects in a population exposed to environmental contaminants differs from that observed in a demographically similar population elsewhere that was not so exposed. More specifically, are residents in the Index Area at increased risk for adverse reproductive outcomes, or for inadequate development during childhood.

The major approach was:

1) The administration of a specifically designed questionnaire for women on their reproductive outcomes, as a supplement to the general health status questionnaire;

2) Inclusion in the medical histories and physical examinations of elements designed to identify the major and some minor birth defects, and major problems in the development of young children.

Three reproductive outcomes were examined that might be adversely affected by exposure to a noxious agent primarily during pregnancy (short-term exposure effects). These are fetal loss, prematurity, low birth weight, and birth defects.

Two others were studied for which the exposure might be cumulative during the whole period of an individual's exposure (long-term exposure effects). These are infertility and inadequate childhood development.

The comparison communities had the same examinations administered and medical examinations performed as in the Index Area, except that insufficient numbers of children under one year of age responded to permit comparisons. Outmigrants were also part of the study on reproductive risks and outcomes.

8. SPECIAL STUDIES IN HEALTH STATUS EVALUATION

8.1 The Trace Metal Studies

Hair was sampled for determination of mercury, arsenic, lead, cadmium, and selenium concentrations, irrespective of age where an adequate amount of hair was present. Blood was sampled for mercury on participants at least 7 years of age.

Analysis of the trace metals was done by the Centre de Toxicologie du Quebec with quality control measures that included random duplicate sample comparisons by the Mayo Clinic.

A trace metal study was also conducted in the Waterton Hutterite Colony, near the Index Area, using a comparison community of the Cameron Farm Colony, near the SR area.

8.2 Lung Function Study

The plausible environmental exposures with potential pulmonary toxicity in the Index Area are the oxides of nitrogen (NO_x), sulfuric acid aerosols and sulphur dioxide (SO_2), and hydrogen sulfide (H_2S).

Spirometry was used to measure lung function because compared to other measures of lung function it is relatively sensitive and specific for respiratory impairment in the context of environmental pollution. Increased airway responsiveness was indicated by response to a bronchodilator.

The general objective was to determine whether or not residents of the Index Area had poorer lung function than residents in other sociodemographically comparable areas of Alberta.

Analysis of results took into account such variables as gender and height, weight, and cigarette smoking.

8.3 Winter Reassessment

A small proportion of study participants believed and informed the Principal Investigator that they were less healthy in the winter season as compared to the summer. The general objective of the reassessment was to determine the extent of seasonal variation on the health status of participants living in the IA and SR area.

The eligible study population was defined as all adult participants in the study during July and August 1985 who were 14 years of age and over from the IA or SR area. From this population a random sample of 225 participants was selected from each of the two areas.

An abbreviated version of the summer questionnaire was administered by a trained interviewer. A shortened version of the summer ritualized medical examination restricted to the head, neck and thorax was performed by a physician who had worked in the summer study. Pre-bronchodilator spirometry was done by two trained technicians. The equipment calibration and methods of testing were identical to those used in the summer study.

9. METHODOLOGICAL RESULTS

9.1 Orientation

This section examines the similarity of the population samples, presents data about the performance of the research team, and gives information about the presence or absence of systematic error or bias that might have complicated interpretation of the main results.

Most importantly, the main control area, SR, was very similar to IA. Also, the DCCI proved to be very similar to SR-M. In Table 9.1/A we show selected sociodemographic characteristics among participants in all areas.

9.2 Conclusions on Methodological Results

1) The similarity of the groups being contrasted was high, both for the samples assembled in the main cross-sectional survey in the summer of 1985 and for the outmigrants who responded to the mail survey.

2) The response rates attained the goals set forth in advance and were similar across the areas, both for the summer survey (IA 92.65%; SR 91.0%; DCCI 90.54%), and the outmigrant follow-up (IA 62.7%; SR 52.8%; DCCI 60.6%).

3) The targets for the Winter Reassessment were met and the subsamples were similar to the samples from which they were drawn and to each other.

4) None of the variables that could have been confounders were sufficiently different among the areas or among the comparison groups to require a statistical adjustment in presentation of the main results. This was remarkably so for lifestyle factors and risk factors connected with hazardous exposure in the work place.

5) Rates of coding accuracy and spot checks of the ritualistic medical examinations all point to a high rate of quality of performance of the interviewing, medical and coding staff.

TABLE 9.1/A*

SELECTED SOCIO-DEMOGRAPHIC CHARACTERISTICS OF PARTICIPANTS

	IA	SR	DCCI	SR-M
Percentage female	49	47	52	46
Mean age adults	42	39	43	39
Mean age children	7	7	6	8
Perc. income 9 to 20,000	20	15	12	13
Perc. education post-secondary or more	23	26	22	24
Perc. occupation farmer	28	25	19	27
Perc. Mormon religion	50	44	1	0
Mean length of residence	27	23	23	21
Perc. in community never smoked	67	61	48	50

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* Incorporates information from Tables 9.2.1.1/1, 9.2.1.2/1, 9.2.1.3/1, 9.2.2/1 in the Main Report.

6) Intra and inter-laboratory differences for the random sample checks revealed good agreement. The main laboratory used for the study (Centre de Toxicologie du Quebec) provides highly repeatable results and reported valid measures of trace metals as shown by their analyses of certified reference specimens calibrated by the Japanese Institute of Environmental Studies.

7) The comparison by area of participants' variables influencing spirometric results reveals that the distribution of influencing factors are close enough to be amenable to adjustment during the analysis of the results in the main study. With respect to the repeatability of the spirometric results the primary outcome variable FEV_1 was proven to be highly repeatable throughout the entire summer.

8) Electrocardiograms showed excellent reproducibility.

10. SUPPLEMENTARY DETAILED INFORMATION ON METHODS

This chapter in the Main Report provides extensive in-depth information about the whole range of procedures, measuring techniques, data management and standards used.

11. RESULTS

11.1 Orientation to Presentation of Results

The main research question asked in this project is whether the people living in the Index Area and exposed to environmental contaminents have different health status than the most comparable and unexposed population within the Province of Alberta. The best reference or control population proved to be the residents in the Stirling/Raymond area (SR area).

Expressed otherwise, the main question of this study concerns a possible "epidemic" of adverse health among people in the Index Area. This study does not explore etiologic or cause/effect in relation to sour gas emissions.

Comparisons with the exposed comparison community of Didsbury/Carstairs/Crossfield/Irricana (DCCI) and with the Stirling/Raymond minus Mormons (SR-M) sample assist in interpretation or corroboration of the main contrasts. This corroboration must be done with caution, however, as there were no prior hypotheses about these ancillary comparisons.

The selected tables that follow in Chapters 12 to 17 in this summary include, when applicable, the specific question in the questionnaire used to gather the data. Interpretation is given in Chapters 18 and 19.

11.2 Statistical Introductory Comments

The following are some of the statistical considerations, which have been the basis for analysis and interpretation of data:

1) In advance, it was declared that "clinical significance" would have to be attained in order to consider the two areas under study (IA vs. SR) as

different for a given health problem. A clinically significant difference is large enough that it cannot be explained either by uncontrollable bias or as trivial effect or both. The level of clinical significance selected a priori was a difference in rates of 10% when the reference rate was less than 10%, and a difference of 20% when the reference rate was greater than 10%.

2) Statistical significance levels (p-values) are infrequently reported in this study because of the very large sizes of the samples.

3) Recognizing that the probability of a statistical error increases with the number of health outcomes compared, the p-values specified in advance as the threshold of statistical significant are lower than usual and generally < 0.01 for two-sided tests.

4) Testing of post-hoc hypotheses (testing the hypotheses after seeing the data) has not been done.

5) The power for detecting differences of 20% or 10% depending on the reference rate is always at least 99.1% for adults and 92.7% for children.

6) The SR area proved to be highly similar to IA, with potential confounding variables such as age, sex, occupation, and life style having only a negligible effect on controllable bias. This justified the presentation of unadjusted results exactly as elicited in the field (i.e. crude instead of adjusted results).

12. OUTMIGRANT FINDINGS RELEVANT TO HEALTH-RELATED SELECTIVE MIGRATION

There has always been concern on the part of the Scientific Advisory Board (SAB), the Community Advisory Boards (CAB) and the investigators about possible selective migration out of the Index Area for reasons determined by health. The result of such selective migration could be that residents living in the Index Area in 1985 might appear to be healthier or less healthy than the SR comparison group.

The outmigrant follow-up (IA, SR and DCCI) was done to determine if such health-related migration had occurred, and, secondly to create the cohorts to measure cancer incidence and the incidence of reproductive outcomes and birth defects.

12.1 Sociodemographic Characteristics

Outmigrants were found to be younger than those who remained in the geographic area studied, their distribution by religion was similar to residents who were still in the original area in 1985, and they had lived less number of years in the areas studied. The relative proportions of IA outmigrants, SR and DCCI outmigrants by sociodemographic variables of interest are similar in magnitude and direction as the corresponding ones for those remaining as residents, especially if one compares IA with SR.

The sociodemographic variables of women of childbearing age show that the outmigrant women are younger than the summer study participants. Their religion distribution is similar to that of those who remained in the geographic area, and their length of residence was similar.

12.2 Comparison of Rates of Illness Among Outmigrants and Summer 1985 Participants

Table 12.2/1 shows that there is a consistent pattern of higher rates of illness for summer participants except for epilepsy and diabetes. Also the ratio IA to SR is similar for the summer 1985 participants and outmigrants in most cases.

Other data indicates that the main reasons for moving were to seek education, seek employment or to establish businesses, for family reasons or to get married. All these predominating reasons are coherent with the fact that younger people moved out. Also, the fact that younger people migrated confirms the observation that they appear to be healthier as reflected in the percentage of illnesses reported in Table 12.2/1.

In all categories of outmigrants, the percentage that moved due to health reasons was very low:

IA(MC)* 1.3%; SR 0.4%; DCCI 1.1%; and SR-M 0%.

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* Index Area first-degree relatives only as is the case in SR and DCCI.

TABLE 12.2/1

COMPARISON OF SELF-REPORTED 1985 ILLNESS AMONG OUTMIGRANTS AND SUMMER PARTICIPANTS (PERCENT)
(15 Years and Over)

	IA*	SR	DCCI	SR-M
N Summer	1390	485	366	290
Outmigrants	599	250	264	132
Heart Disease				
Summer	13.6 (13.4)**	11.8 (11.3)	9.6 (9.6)	10.7 (10.0)
Outmigrants	2.3	1.2	1.5	0.8
Hypertension				
Summer	21.1 (20.8)	15.5 (15.3)	23.2 (23.1)	16.6 (16.2)
Outmigrants	5.2	3.2	3.8	4.6
Migraine				
Summer	12.6	8.3	9.3	6.6
Outmigrants	7.4	6.4	4.2	5.3
Epilepsy				
Summer	0.3	0.4	0.8	0.3
Outmigrants	1.7	0.4	1.5	0.0
Chronic Bronchitis of Phlegm > 1yr				
Summer	20.3 (4.3)	13.6 (3.5)	19.1 (5.0)	14.5 (3.8)
Outmigrants	4.3	2.4	1.9	1.5
Chronic Lung Disease (Emphysema)				
Summer	0.8	0.0	1.1	0.0
Outmigrants	1.0	0.4	0.0	0.0
Diabetes				
Summer	2.7	1.4	1.9	1.7
Outmigrants	2.2	2.0	1.1	3.0

* For outmigrants, this area includes only people who are first degree relatives of the contact person.

** Numbers in brackets correspond to summer sample people with a positive response to the direct question "Were you ever told by a doctor that you had (illness names)". This formulation is most similar to that which is asked in the outmigrant questionnaire.

13. HEALTH STATUS EVALUATION

In this chapter, variables which are conventional indicators of the health status of a population are reviewed. The majority of these are based on information supplied by respondents, and are therefore subjective. Some of them have been verified with data from independent sources.

The indicators studied included physical disability, utilization of health services (with caution due to questions of access and availability), prevalence of major, chronic irreversible illness, burdens of symptoms (subjective; information from participants), burden of signs (observations made by physicians), laboratory findings, rates of diagnosed diseases, and cardinal outcomes.

The focus has been on cardinal outcomes of health, which include the symptoms, signs, and diagnoses that are most plausibly associated with the environmental risk factors of concern in the Index Area. All cardinal symptoms, signs and diagnoses were declared before the field work began and documented before the analysis began.

13.1 Current Physical Disability

Data regarding the percentage of adults free of any activity loss during the last two weeks, shows a 3.9% higher percentage in SR (82.3%) compared to IA (78.4%). There is no difference between DCCI and SR-M. When considering the percentage of persons free of bed disability in the preceding two weeks the results are similar across the four samples. When data on freedom from activity loss and bed disability in the last two weeks is analyzed for percentage of days rather than the percentage of persons, there are no differences across all the samples.

As seen in Table 13.1.1/5, the number of bed-days per thousand persons was slightly higher in the IA as compared to SR for persons under 65 years of age, while it was markedly higher in SR as compared to IA in those 65 years of age or over. Males had much more bed disability in SR than IA, while for women the rates are more comparable. When the groups are combined, there is a greater number of bed-days in SR than IA. It should be noted that data from the Canada Health Survey are included in the table. The bed disability experience for IA is noted to be somewhat lower than Canada as a whole, somewhat higher than the Prairies and appreciably lower than for a reference area of Toronto.

13.2 Utilization of Health Services

Table 13.2.1/1 presents the percentage of persons spending at least one night in any health care facility during the preceding 12 months. Men were somewhat more likely to have spent a night in hospital in the IA compared to SR. All areas we studied in Alberta show appreciably higher use of institutional health care facilities than urban Toronto (TC) or Canada as a whole.

Results for all areas are similar and somewhat lower than the Canadian experience for the percentage of adults reporting a medical problem and having an encounter with a health professional in the last two weeks. The percentages were 14.3% for IA and 13.2% for SR. The Canadian average is 15.5%.

For medicine taken on the advice of a medical doctor, the percentages are almost identical when comparing IA (37.8%) with SR (37.5%). In contrast, for medicines taken without the advice of a medical doctor, the difference is 6.4% greater in IA. Considering all medications, whether prescribed or not, there are no important differences, IA being 64.7% and SR 62.1%.

TABLE 13.1.1/5

TWO WEEK BED DISABILITY
(MEAN NUMBER OF DAYS PER 1,000 PERSONS)
(15 Years and Over)

	AREA						
	IA	SR	DCCI	SR-M	TC	(CHS)* CANADA	(CHS)* PRAIRIES
N	1386	482	366	287	261	2433	335
15 - 64 years	166	150	110	106		164	94
65+ years	109	773	121	272		548	375
Male	68	132	69	91		139	55
Female	252	293	152	150		281	215
Combined	158	207	112	118	309	212	137

* From average number of bed days per person for two week period in July 1978.

Question 12A: HOW MANY DAYS DID YOU STAY IN BED FOR ALL OR MOST OF THE DAY, INCLUDING ANY NIGHTS SPENT AS A PATIENT IN HOSPITAL (IN THE LAST 2 WEEKS)?

TABLE 13.2.1/1

PERCENTAGE OF ADULTS SPENDING AT LEAST ONE NIGHT IN ANY HEALTH CARE FACILITY* IN THE LAST TWELVE MONTHS
(15 Years and Over)

	AREA					
	IA	SR	DCCI	SR-M	TC	CHS**
N	1387	484	366	289	261	17492
15-64 years	18.8	16.6	13.0	14.2		9.8
65+ years	24.8	25.0	29.3	22.7		18.3
Male	16.2	11.2	12.6	9.0		7.7
Female	23.3	24.4	18.3	21.8		13.8
Combined	**19.7**	**17.4**	**15.6**	**14.9**	6.5	10.8

* Participants in the MDR study reported nights in a hospital only; no one spent time in a nursing home or convalescent home in the last 12 months.

** Respondents by hospital stay in at least 12 months.

Question 15: IN THE PAST 12 MONTHS, WERE YOU A PATIENT IN A HOSPITAL, A NURSING HOME OR A CONVALESCENT HOME?

It should be noted that the percentage of respondents in all four Alberta areas using one or more drugs in the last two days is appreciably higher than Canada (48.9%) as a whole and for an unexposed area of Toronto (49.2%). When assessing the average number of medications taken per person in the preceding two days, the figure was 1.2 per person in IA and 1.1 in SR. Canadians in general, when asked the question in an identical manner used 0.8 medications per day and urban Toronto residents 1.0. There are no differences between IA and SR when reviewing the percentage of children who used one or more medications in the preceding two days. However, the rates for children are more comparable to those of urban Toronto and Canada as a whole. When considering the mean number of medications taken per child per day, essentially in all areas, each child takes about 1/2 a medication per day.

13.3 Prevalence of Major Chronic Irreversible Illness

There are no clinically significant differences in the prevalence of self-reported irreversible illnesses (eyesight problems not corrected by glasses, diabetes, epilepsy, heart disease, kidney disease) among the residents of IA compared to SR. All Alberta areas have rates somewhat lower than the urban Toronto reference area. The prevalences of diabetes and heart disease are similar to those of all of Canada as reported by the CHS. The Alberta rates were also similar to the Toronto rates.

Table 13.3/2 shows the prevalence of musculoskeletal ailments for adults. There are higher rates for IA compared to SR and also for DCCI compared to SR-M for "trouble with limbs and/or other bones or joints". The differences with regard to "trouble with the back or spine" across the four areas were slight.

TABLE 13.3/2

PREVALENCE OF MUSCULO-SKELETAL AILMENTS
ADULTS
(15 Years and Over)

	AREA			
	IA	SR	DCCI	SR-M
N	1387	485	366	290
% Responding "yes" to any of the following:				
- Trouble with the* back or spine	41.0	38.0	37.4	38.6
- Trouble with the** limbs and/or other bones or joints	52.3	42.3	47.5	40.3

* Yes response to 20(13).
** Yes response to any of 20(14), (15), or (16).

Question 20: DO YOU PRESENTLY HAVE:
13) TROUBLE WITH THE BACK OR SPINE?
14) TROUBLE WITH THE LEGS OR HIPS?
15) TROUBLE WITH THE ARMS OR SHOULDERS?
16) TROUBLE WITH ANY OTHER BONES OR JOINTS?

13.4 Clinical Findings

Clinical findings were elicited by questionnaire, physical examination, and laboratory investigation.

13.4.1 General Morbidity

13.4.1.1 Prevalence of Health Problems

The two-week prevalences of any health problem reported spontaneously by participants are similar across the four areas for men and women combined. Differences are not clinically significant. (IA 30.1%; SR 26.2%). Similarly, for children there is no clearcut pattern, rates are similar and no differences have clinical significance. It is interesting to note that the rates for combined men and women in all Alberta areas are lower than for TC in Toronto and appreciably lower in Alberta children compared to Toronto children.

13.4.1.2 Paraclinical and Laboratory Findings

The following is a summary of key findings:

1) Measured visual acuity - the difference between IA and SR was less than 1%.

2) Urinalysis - the percentage of participants free of all measured urinary abnormalities were as follows:

   89.8% for IA; 90.7% for SR; 93.1% for DCCI; and 93.4% for SR-M.

3) Blood samples - the overall findings were summarized by measuring the percentage of participants free of all measured biochemical abnormalities:

   45.4% for IA; 43.4% for SR; 46.4% for DCCI; and 43.8% for SR-M.

4) Electrocardiogram - a summary of these results as indicated by the percentage of participants with any abnormality:

22.1% for IA; 23.5% for SR; 22.8% for DCCI; and 23.0% for SR-M.

13.4.1.3 Rates of Diagnosed Disease

Taking into account all diagnoses written by physicians in judgemental examinations, supplemented by information from consultations in university hospitals, Table 13.4.1.3/1 shows, by rank, the most frequent diagnoses. By far the most common finding was "ostensibly healthy" with the SR showing 5.1% more individuals in that category than IA; SR-M had a 5.4% higher prevalence of such individuals than DCCI.

The results derived from formal clinical algorithms which used data from the questionnaire, ritualized physical examination, and laboratory to define specific conditions are presented in Table 13.4.1.3/2. Overall specific conditions had higher prevalences in IA as compared to SR, and there was a slight trend for DCCI to have higher prevalences than SR-M.

In data which compares the period prevalence of recorded illnesses in the 1970 cohorts of the four study areas, no important differences are detected in these outmigrant groups between the IA and SR with respect to heart disease, migraine, epilepsy, chronic lung disease or diabetes. There is a 7.5% higher rate in the period prevalence of hypertension among the Index Area 1970 cohort as compared to SR, and a 5.6% elevation in the period prevalence of chronic bronchitis (with phlegm lasting more than one year) between these two groups. Although technically the differences in rates of report of these two conditions did not attain clinical significance the investigators "flagged" them for in-depth analysis given the population importance of hypertension and chronic bronchitis.

TABLE 13.4.1.3/1

PERCENTAGE OF ALL PARTICIPANTS WITH MOST COMMON DIAGNOSES MADE BY JUDGEMENTAL AND CONSULTING PHYSICIANS

	AREA			
	IA	SR	DCCI	SR-M
N	2148	821	616	458
Ostensibly healthy	54.0	59.1	50.5	55.9
Uncomplicated hypertension	9.1	7.4	9.3	8.1
Hay fever, allergic rhinitis	8.4	6.9	4.2	8.5
Obesity	5.2	3.7	3.4	3.5
Asthma	3.9	3.4	4.4	2.6
Chronic bronchitis	2.6	3.2	3.6	4.2
Deafness, not otherwise specified	3.1	1.6	1.8	1.8
Osteoarthritis	2.1	1.6	5.0	1.5
Status-post surgery	2.8	2.0	2.1	2.2
Conjunctivitis	2.5	2.1	2.4	2.6

TABLE 13.4.1.3/2

PERCENTAGE OF PARTICIPANTS WITH SPECIFIC CONDITIONS DEFINED BY FORMAL CLINICAL ALGORITHMS: RESULTS ARE PRESENTED BY AREA*

CONDITION		AREA			
		IA	SR	DCCI	SR-M
N		1383	465	348	276
OCULAR					
conjunctivitis	probable	29.4	22.6	23.9	26.1
	definite	1.4	1.5	1.4	1.1
RESPIRATORY					
rhinitis	probable	19.2	13.3	15.2	14.5
	definite	3.2	3.9	2.6	4.7
pharyngitis	probable	21.4	13.8	18.4	17.8
	definite	0.9	3.2	0.9	2.9
chronic bronchitis		12.4	8.6	12.4	9.4
wheezing syndromes	grade 1***	14.2	13.6	16.4	13.8
	grade 2	4.3	2.4	4.6	2.9
	grade 3	2.8	2.4	2.3	2.5
OCULAR AND RESPIRATORY IRRITATION COMBINED**		24.7	20.8	21.0	23.9
CUTANEOUS					
dermatitis	possible	11.5	12.3	14.1	11.6
	probable	2.8	1.5	1.2	2.5
	definite	4.0	2.4	2.3	1.8

* Results based on 2,196 subjects ≥ 15 years of age who had a questionnaire, physical examination, and laboratory data available for analysis. The diagnostic algorithms used, due to their length, have been put into Appendix 5.1.6.

** Percentage of participants with at least one of definite conjunctivitis, rhinitis, definite pharyngitis, or chronic bronchitis.

*** Grade of severity of wheezing syndrome.

TABLE 13.4.1.3/2 (CONTINUED)

PERCENTAGE OF PARTICIPANTS WITH SPECIFIC CONDITIONS DEFINED BY FORMAL CLINICAL ALGORITHMS: RESULTS ARE PRESENTED BY AREA*

CONDITION	AREA			
	IA	SR	DCCI	SR-M
N	1379	464	344	275
NEUROLOGICAL				
symptomatic polyneuropathy	0.3	0.2	0.3	0.0
asymptomatic polyneuropathy	0.5	0.0	0.6	0.0
mononeuropathy				
sensory component	1.2	1.1	0.3	0.4
motor component	0.5	0.7	0.6	0.7
essential tremor	0.3	0.2	0.6	0.0
combined neurological***	2.7	1.5	2.0	0.7
OTHER RELATIVELY FREQUENT CONDITIONS				
HYPERTENSION	9.7	7.3	9.2	6.5
complicated****	4.2	1.7	2.9	1.4
OBESITY	37.4	36.3	35.3	33.7
DEAFNESS				
one ear	3.8	5.2	2.3	5.1
both ears	4.5	2.4	3.5	1.8
BACK PAIN				
any back pain	30.7	34.1	33.0	35.5
with any neurological signs	10.3	4.7	6.1	4.4
HEART MURMUR				
systolic only	15.6	12.0	14.9	10.9
diastolic with or without systolic	0.7	0.9	0.0	1.5

*** Percentage of participants with at least one of; motor or sensory neuropathy, symptomatic or assymptomatic polyneuropathy, or essential tremor.

**** Result based on 1739 subjects ≥25 years of age who had a questionnaire, physical examination, laboratory data, and an elective cardiogram available for analysis.

13.4.2 Cardinal Outcomes

13.4.2.1 Cardinal Symptoms

When comparing IA and SR for the two-week period prevalence of cardinal symptoms (subjective information provided by participants), there is a trend, in most of the symptoms, of higher percentages among residents of the IA--among both adults and children. (Table 13.4.2.1/1 and Table 13.4.2.1/2). In the comparisons between DCCI and SR-M the findings are more similar without any trend favouring either group.

Table 13.4.2.1/3 shows the two-week prevalence of at least one probed cardinal symptoms among 15 considered important. Prevalences are slightly higher for both adults and children in the IA compared to SR. Any differences between DCCI and SR-M are inconsequential, clinically.

13.4.2.2 Cardinal Signs

As seen in Table 13.4.2.1/4, when comparing the percentages of objective cardinal physical signs observed in participants, by physicians, there are no clinically significant differences in any of the contrasts between IA and SR. Neither are there any such differences between the DCCI and the SR-M. For this group of variables, whether one considers the proportion of persons without any signs at all or conversely those with at least one sign, there is a trend for the IA to have less signs than the SR. Similarly, the exposed DCCI area has less signs than the SR-M.

As seen in Table 13.4.2.1/5, when considering specific cardinal physical signs frequently observed by physicians in the medical ritualistic examination, there are no differences for any of the cardinal signs. Red eyes and red mucosa were observed at lower rates both in IA and DCCI compared to their reference population.

13.4.2.3 Cardinal Diagnoses

Table 13.4.2.1/6 shows that there are no important differences between IA and SR in the percentage of most frequent cardinal diagnoses by area.

13.4.3 Additional Health Status Indicators

13.4.3.1 Mental Health Status

Using a "screening" data-gathering instrument, residents in all areas were found to be very near the maximum attainable level of healthy mental status.

13.4.3.2 Perception of Community Health Hazards

Participants were asked if there were anything in the community where they lived which they felt or perceived would affect their health in any way (Table 13.4.3.2/1). The rate answering "yes" in IA is one third higher compared to SR. The question was phrased in order not to be leading, and there is an unlikely possibility that some of those responding "yes" in IA felt that there were factors affecting their health in a beneficial way. However, that is very unlikely given the known general concerns in the community. It is curious to notice that in DCCI, the percentage of those responding "yes" is almost exactly the same as in the unexposed SR-M even though the exposure of DCCI participants is very similar to that in IA.

TABLE 13.4.2.1/1

TWO WEEK PERIOD PREVALENCE OF CARDINAL SYMPTOMS
ADULTS
(15 Years and Over)

	AREA			
	IA	SR	DCCI	SR-M
N	1390	485	366	290
Ocular Symptoms				
Itching, burning or watering of eyes	30.7	24.1	24.9	27.2
Respiratory Symptoms				
Itching, burning or running nose not due to a cold	22.3	16.7	17.5	18.6
Irritation of the throat not due to a cold	22.2	16.5	18.3	20.0
Feeling of suffocation	11.9	8.3	7.7	9.3
Shortness of Breath	23.5	20.2	21.0	20.0
Cough	26.5	25.6	28.8	27.9
Phlegm	26.4	22.1	22.7	19.0
Wheezing	10.6	9.9	10.9	10.0
Cutaneous Symptoms				
Burning or itching of the skin	18.3	15.9	16.9	15.9
Neurological Symptoms				
Weakness of hands, feet, fingers, or toes	8.4	6.2	6.8	7.6
Loss of feeling in the hands, feet, fingers, or toes	9.8	4.5	6.0	5.2
Tingling in the hands, feet, fingers, or toes	17.9	10.9	13.9	8.6
Trembling of the hands	14.0	11.1	12.0	10.7
Gastro-Intestinal Symptoms				
Nausea	16.8	15.5	10.7	14.8
Other Symptoms				
Tiredness or Fatigue	33.8	28.3	30.1	27.9

TABLE 13.4.2.1/2

TWO WEEK PERIOD PREVALENCE OF CARDINAL SYMPTOMS
CHILDREN
(1 - 14 Years)

	AREA			
	IA	SR	DCCI	SR-M
N	726	341	263	170
N	527*	228*	158*	141*
%				
Ocular Symptoms				
Itching, burning or watering of eyes	15.7	10.6	10.7	9.4
Respiratory Symptoms				
Itching, burning or running nose not due to a cold	16.7	11.4	10.3	13.5
Irritation of the throat not due to a cold	12.3	9.1	8.8	9.4
Feeling of suffocation	4.1	2.1	2.7	2.4
Shortness of Breath*	4.6	3.1	3.8	3.6
Cough	11.9	10.3	8.4	8.8
Phlegm	7.3	5.9	3.7	4.9
Wheezing	5.1	3.8	3.8	4.1
Cutaneous Symptoms				
Burning or itching of the skin	11.3	11.7	9.9	11.2
Neurological Symptoms				
Weakness of hands, feet, fingers, or toes*	2.1	1.8	0.6	2.1
Loss of feeling in the hands, feet, fingers, or toes*	0.2	0.4	0.6	0.7
Tingling in the hands, feet, fingers, or toes*	1.5	2.6	0.6	2.8
Trembling of the hands*	2.7	2.2	1.3	2.1
Gastro-Intestinal Symptoms				
Nausea	16.7	16.7	17.9	16.5
Other Symptoms				
Tiredness or Fatigue	14.6	12.9	14.1	12.9

* Not elicited for children ages 1 - 4.

TABLE 13.4.2.1/3

TWO WEEK PERIOD PREVALENCE OF AT LEAST ONE PROBED CARDINAL SYMPTOM

(Out of 15)*

	AREA			
	IA	SR	DCCI	SR-M
Adults (15+) N	1392	485	364	290
Male	76.1	70.9	71.3	71.6
Female	83.4	78.0	77.4	78.5
Combined	**79.4**	**74.2**	**74.3**	**74.8**
Children (1-14)** N	726	341	263	170
Male	52.8	47.5	51.5	49.4
Female	48.4	45.3	46.6	42.2
Combined	**50.7**	**46.3**	**49.1**	**45.9**

* See list in previous table.
** Ten symptoms only available for children ages 1-5.

TABLE 13.4.2.1/4

PREVALENCE OF CARDINAL PHYSICAL SIGNS IN PARTICIPANTS

	AREA			
	IA	SR	DCCI	SR-M
N	2151	816	616	454
Percentage with:				
No signs	63.5	54.8	69.6	54.0
One sign	25.6	33.1	23.4	33.5
At least one sign	36.5	45.2	30.4	46.0

TABLE 13.4.2.1/5

PERCENTAGE OF SPECIFIC SELECTED CARDINAL PHYSICAL SIGNS OBSERVED IN MEDICAL RITUALISTIC EXAMINATION

	AREA			
	IA	SR	DCCI	SR-M
N	2151	816	616	454
Red Eyes	10.7	17.5	8.8	18.7
Red Mucosa	12.8	24.5	10.4	23.6
Wheezing and crackles in lungs	2.8	2.6	1.8	3.1
Skin rash	3.8	2.3	2.1	2.4
Ear drum abnormalities	9.3	7.5	8.0	7.7
Neurological findings	11.9	7.1	7.6	7.3
Tremor	0.6	0.0	0.7	0.0

TABLE 13.4.2.1/6

PERCENTAGE OF MOST FREQUENT CARDINAL DIAGNOSES BY AREA FROM MEDICAL JUDGEMENTALS AND CONSULTATIONS

	AREA			
	IA	SR	DCCI	SR-M
N	2148	821	616	458
Hay fever, allergic rhinitis	8.4	6.9	4.2	8.5
Asthma	3.9	3.4	4.4	2.6
Chronic bronchitis	2.6	3.2	3.6	4.2
Conjunctivitis	2.5	2.1	2.4	2.6
Dermatitis Not Otherwise Specified	2.7	0.6	2.8	0.7
Peripheral neuropathy and cerebral palsy	2.0	2.6	1.6	1.8
Other diseases of the eye	2.1	1.0	2.4	1.5
Upper Respiratory Tract Infection	1.5	2.0	2.6	1.5
Other diseases of the skin	0.9	0.9	2.4	0.7
Acne	0.9	1.2	1.5	2.2
Congenital anomalies	1.6	1.7	1.0	2.2
Allergic reactions	1.1	0.4	1.1	0.4
Sinusitis acute & chronic	1.0	0.4	0.0	0.7
Urticaria	0.8	0.0	0.3	0.0
Abnormal urine test	0.7	0.7	0.0	0.7
Dyspnea	0.5	0.4	0.7	0.2
Psoriasis	0.5	0.4	0.5	0.4
Emphysema, Chronic Obstructive Pulmonary Disease	0.6	0.1	0.2	0.0
Benign neoplasm of skin	0.2	0.0	1.3	0.0

TABLE 13.4.3.2/1

PERCEPTION OF PARTICIPANTS REGARDING FACTORS IN THE COMMUNITY WHICH MAY AFFECT THEIR HEALTH (15 Years and Over)

	AREA			
	IA	SR	DCCI	SR-M
N	1269	473	362	285
% answering "yes"	20.1	13.5	13.3	13.3

Question 80 (c): IS THERE ANYTHING IN THE COMMUNITY WHERE YOU LIVE THAT AFFECTS YOUR HEALTH IN ANY WAY?

14. SPECIAL STUDIES IN HEALTH STATUS EVALUATION

14.1 Trace Metal Study

Table 14.1/2 presents trace metal values categorized according to an a priori laboratory classification. For all participants combined, greater than 94% of values were either within the undetectable (UD) or normal (NN) range. IA as compared to SR had an equal or lower percentage of people with high (HH) results for every trace metal determination. This relationship continued to hold if those with borderline (NH) were combined with HH results with the exception of blood mercury. DCCI as compared to SR-M had an equal or lower proportion of people with HH results for each trace metal determination and this relationship persisted when NH and HH results were combined with the exception of hair arsenic.

14.2 Trace Metal Study of Hutterites

Among Hutterites, blood mercury, hair arsenic and hair cadmium values were all within the normal range. The Index Area Hutterites (HUT-IA) as compared to the SR area Hutterites (HUT-SR) had slightly greater levels of hair lead and selenium. For all trace metals, HUT-IA as compared to IA had similar proportions within each category of NH and HH except for the HH category of hair selenium which was approximately 9% higher in HUT-IA as compared to SR. For all trace metals, HUT-SR as compared to SR had similar proportions within each category of NH and HN except for the NH category of hair lead which was approximately 4% lower in HUT-SR as compared to SR.

14.3 Summary of Spirometric Results Obtained During Health Status Evaluation of Respiratory System

Only the primary outcome variable for respiratory function, the one-second forced expired volume (FEV_1) is presented in this

TABLE 14.1/2

TRACE METAL VALUES FOR ALL PARTICIPANTS COMBINED AND BY AREA RESULTS ARE EXPRESSED AS THE PERCENTAGE OF PARTICIPANTS WITH VALUES IN EACH OF FOUR CATEGORIES DEFINED ACCORDING TO AN A PRIORI LABORATORY CLASSIFICATION*

Trace Metal	Area	Number	Laboratory Classification			
			UD	NN	NH	HH
Mercury (blood) ug/L	Combined	2835	5.7	93.8	0.5	0.0
	IA	1746	7.4	92.0	0.6	0.0
	SR	637	2.7	96.9	0.5	0.0
	DCCI	452	3.5	96.5	0.0	0.0
	SR-M	387	2.6	96.6	0.8	0.0
Mercury (hair) ug/gm	Combined	3302	8.2	87.7	3.7	0.4
	IA	1967	10.9	85.7	3.0	0.4
	SR	760	4.3	90.5	4.7	0.4
	DCCI	575	4.0	91.0	4.9	0.2
	SR-M	428	4.4	90.0	5.4	0.2
Arsenic (hair) ug/gm	Combined	3302	78.6	21.2	0.1	0.0
	IA	1967	80.3	19.6	0.1	0.0
	SR	760	78.3	21.6	0.0	0.1
	DCCI	575	73.4	26.3	0.4	0.0
	SR-M	428	78.5	21.3	0.0	0.2
Cadmium (hair) ug/gm	Combined	3302	22.7	77.1	0.0	0.2
	IA	1967	27.9	72.1	0.0	0.1
	SR	760	13.7	86.1	0.0	0.3
	DCCI	575	17.2	82.4	0.0	0.4
	SR-M	428	13.8	85.8	0.0	0.5
Lead (hair) ug/gm	Combined	3302	15.4	78.9	4.6	1.1
	IA	1967	17.5	77.8	3.7	1.0
	SR	760	12.1	80.7	5.5	1.7
	DCCI	575	12.2	80.4	6.6	0.9
	SR-M	428	12.4	79.0	6.5	2.1
Selenium (hair) ug/gm	Combined	3302	6.6	89.9	0.0	3.5
	IA	1967	8.3	88.2	0.0	3.5
	SR	760	4.9	91.6	0.0	3.6
	DCCI	575	3.1	93.4	0.0	3.5
	SR-M	428	2.8	93.7	0.0	3.5

* For trace metal values associated with laboratory ranges see Table 14.1/3

UD = Concentration is undetectably low

NN = Concentration within expected range according to both the Quebec Centre de Toxicologie and the Mayo Clinic.

NH = Concentration within expected range for one laboratory and higher than the expected range for the other laboratory. For hair and blood Mercury, NH designates values that lie between expected and high for both laboratories.

HH = Concentration higher than the expected range according to both laboratories.

section. Extensive results showing results of forced vital capacity (FVC), of mid-maximal expiratory flow (MMEF), of bronchodilator response and of chronic airflow limitation are presented in crude and adjusted manner.

Summarizing the results in children, FEV_1 results both unadjusted and adjusted, were very similar across all areas, for the most part within one standard error of one another. Because of the large sample sizes, the standard errors are very small. There was a slight trend for the FEV_1 to be higher (showing better pulmonary function) in IA than SR. Summarizing the results of adults, FEV_1 values once adjusted for influencing factors, such as smoking, were similar among all four areas. When the results were internally adjusted, IA was equal to SR and DCCI was lower than SR-M by less than one standard error. These trends were consistent with those found by external adjustment.

14.4 Winter Reassessment

From summer to winter in both IA and SR there was an approximate 15% change (increase) in the two week period prevalence of reported health problems. These differences were similar in magnitude and direction for both IA and SR.

Probed symptoms were those elicited by direct questioning and were related to ocular, respiratory, cutaneous, neurological and gastrointestinal symptoms, as well as tiredness or fatigue. IA demonstrated a 2.5% increase in probed symptoms while SR demonstrated a 1.8% decrease. The absolute difference in magnitude of summer/winter differences between areas was 4.3%.

7% of IA participants and 12% of SR participants reported the occurrence of a new health event occurring since the summer, with the difference between the two areas being 5%. SR showed a larger increase in symptoms than IA.

For the two week period prevalence percent of specific cardinal symptoms (known to be or could plausibly be related to airborne environmental and/or other irritant exposure), in general, less participants reported symptoms during the winter than during the summer. The exceptions were an increase in cough and phlegm (IA and SR), skin irritation (IA only), tingling of extremities (IA only), trembling of hands (SR only) and nausea (SR only). Summer/winter differences in the two areas were in general similar both in magnitude and direction.

Summer/winter differences for cardinal physical signs (physical detected signs associated with or plausibly associated to sour gas exposure and/or airborne irritants) were small and inconsistent with the following two exceptions: a 9% decrease in participants with red nasal mucosa in SR and a 9.6% decrease in eardrum abnormalities in IA. With respect to red mucosa, the magnitude of the difference between IA and SR summer/winter difference is approximately 10%. (i.e. IA +1.3% summer/winter difference; SR -9.1% summer/winter difference).

The Winter Reassessment samples, as compared to the total summer study groups from which they were drawn have similar proportions of participants reporting cardinal signs; the largest difference was a 4.8% greater proportion of the IA winter subsample reporting at least one sign. For the report of at least one sign, a 3.8% increase from summer to winter in IA was present with a 6.1% decrease in SR.

For respiratory function as shown in Table 14.4/7 for the outcome variable, FEV_1, MMEF and FVC, the summer/winter differences were comparable between IA and SR.

TABLE 14.4/7

RESPIRATORY FUNCTION DIFFERENCES BETWEEN JULY/AUGUST 1985 AND JANUARY 1986. MEAN RESULTS ARE PRESENTED FOR ALL WINTER PARTICIPANTS COMBINED AND BY AREA

	N	Summer	Winter	Summer-Winter Change	
FEV_1 (L)				Mean	Percentage
Combined	326	3.49 (.05)*	3.44 (.05)	-.05	-1.5
IA	166	3.44 (.07)	3.38 (.07)	-.06	-1.6
SR	160	3.55 (.06)	3.50 (.06)	-.05	-1.3
MMEF (L/sec)					
Combined	326	3.28 (.07)	3.15 (.07)	-.13	-3.5
IA	166	3.18 (1.34)	3.00 (1.37)	-.18	-5.6
SR	160	3.40 (1.26)	3.31 (1.21)	-.08	-1.4
FVC (L)					
Combined	326	4.45 (.06)	4.42 (.06)	-.04	-0.8
IA	166	4.40 (.09)	4.38 (.09)	-.02	-0.3
SR	160	4.51 (.08)	4.45 (.08)	-.06	-1.3

Definition of Abbreviations:
FEV_1 = second forced expiratory volume
FVC = forced vital capacity
MMEF = mid-maximal expiratory flow

* Standard error

15. CANCER RISKS AND OUTCOMES

15.1 Results of Primary Analyses

15.1.1 Person-Years of Risk

Chapter 6 details the methods for the study of cancer risk and outcomes.

Person-years of risk by age group and time interval for the Index Area 1970 cohort males and females were determined. A total of 30,175 person-years of risk were experienced by the entire Index Area 1970 cohort; this is remarkably close to the estimate of 30,000 derived in the a priori sample size calculations.

15.1.2 Incidence Rates for Reference Populations

Incidence rates, by age group and time interval, were derived from Alberta Cancer Registry data for the reference populations. Standardization was performed using the 1976 Alberta male population. Consideration of these standardized rates indicates that the cancer incidence is remarkably similar among the three reference populations and that, as might be anticipated, the cancer incidence rates have risen in a uniform fashion in all three populations with time.

An analogous set of incidence rates for females in the reference populations was determined. Standardization was also done with the 1976 Alberta female population. Again, the incidence rates were similar among the three reference populations and a general trend of increasing incidence with time is noted.

15.1.3 Incident Cancers

A total of 123 incident cancers was identified among the Index Area 1970 cohort during the period 1970-84. (Table 15.1.3/1).

Among the RG (Resident Group as of summer of 1985) a total of 35 cancers were identified occurring in 34 individuals (one individual had 2 cancers). Of the 35 incident cancers, 20 were non-melanotic skin cancers while the remaining 15 were distributed among the various types of malignancies as shown in the table. It is noteworthy that only 29 of these 35 cancers were reported by the RG member at the time of the health study. The additional 6 cancers were identified solely through linkage with the Alberta Cancer Registry. In 5 of 6 of these unreported cancers, the diagnosis was non-melanotic skin cancers, while in the sixth instance, a cancer of the bladder was unreported.

A total of 88 incident cancers were identified in the OG (Outmigrant Groups) occurring in 75 individuals; there were 64 individuals with 1 incident cancers, and 1 individual with 4 incident cancers. Of the 88 cancers in the OG, a total of 25 were innocuous non-melanotic skin cancers while the remaining 63 were distributed as shown in Table 15.1.3/1.

Consideration of the 123 incident cancers among the IA 1970 cohort and their distribution as seen in the right hand column of the table leads to two observations. First no less than 45 of the 123 cancers (37%) were non-melanotic skin cancers. Second, one cannot help but be struck by the paucity of respiratory cancers in this group.

15.1.4 Standardized Incidence Ratio Analysis

The standardized incidence ratio analysis is the primary test of hypothesis in this study. The results of this analysis are presented in Table 15.1.4/1. In the first analysis, non-

TABLE 15.1.3/1

INCIDENT CANCERS AMONG THE INDEX AREA 1970 COHORT DURING THE PERIOD 1970-84

	Resident Group		Outmigrant Group		Total
TYPE (ICD-9)	Male	Female	Male	Female	
Gastro-intestinal (150.0 - 150.9)	1	2	10	5	18
Breast (174.0 - 175.9)	0	3	0	6	9
Respiratory (160.0 - 165.9)	0	0	4	2	6
Kidney, Bladder, Prostate (185.0 - 189.9)	4	1	17	3	25
Gynecologic (179.0 - 184.9)	0	1	0	4	5
Lip, Oral, Pharynx (140.0 - 149.9)	2	0	3	0	5
Bone, Soft tissue (170.0 - 171.9)	0	0	0	1	1
Lymphoid, Leukemia (200.0 - 208.9)	0	0	0	1	1
Melanoma (172.0 - 172.9)	0	1	0	1	2
Other (190.0 - 199.9)	0	0	3	3	6
Skin (non-melanoma) (173.0 - 173.9)	10	10	17	8	45
TOTAL	17	18	54	34	123

TABLE 15.1.4/1

STANDARDIZED INCIDENCE RATIOS (SIR) EXCLUDING NON-MELANOTIC SKIN CANCER FOR THE INDEX AREA 1970 COHORT RELATIVE TO THE THREE REFERENCE POPULATIONS

Population	Observed	Expected*	Expected**	Expected***
Index Area 1970 Cohort Males	45	49.6	49.6	52.7
Index Area 1970 Cohort Females	33	36.3	34.2	35.1
Index Area 1970 Cohort Total	78	85.9	83.8	87.8
SIR* (95% CI)		0.91 (0.67, 1.26)		
SIR** (95% CI)			0.93 (0.68, 1.29)	
SIR*** (95% CI)				0.89 (0.65, 1.23)

* Southern Alberta excl. Calgary, Lethbridge, & Medicine Hat (RP1)
** Census Division 6 excl. Calgary (RP2) - contains DCCI
*** Census Division 2 excl. Lethbridge (RP3) - contains SR

melanotic skin cancers have not been included as these are lesions which seldom if ever lead to serious morbidity or mortality.

The standardized incidence ratio analysis is presented in the table's bottom panel. There were a total of 78 incident cancers in the IA 1970 cohort. Based on the three reference populations, the expected numbers of cancers were 85.9, 83.8 and 87.8, respectively. These data give rise to standardized incidence ratios of 0.91, 0.93 and 0.89 respectively. The 95% confidence intervals provided for each standardized incidence ratio indicate that these ratios are not statistically significantly different than unity. Unity means exactly equivalent observed and expected cancers.

To test the contribution of non-melanotic skin cancers on the results, a second standardized incidence ratio analysis was done. Even with the inclusion of non-melanotic skin cancers, in no case is the standardized incidence ratio statistically significantly different than unity.

To summarize the results of the first analysis, the investigators detected no excess in overall cancer experienced by the Index Area 1970 cohort during the Incidence Period. The data suggest that the overall cancer experience of this cohort during the period 1970-84 is remarkably similar to that which should be expected based on the 3 reference populations from Southern Alberta.

15.2 Results of Secondary Analyses of the Cancer Data

Several analyses were done to test for the presence of bias, to test the effect of inaccurate information, and to provide ancillary data.

After secondary analyses the investigators concluded that:

1) Any inaccuracies in information about a small number of outmigrants could not have caused a failure to detect a significant increase in cancers;

2) Even when individuals with maximal duration of exposure are considered, in order to balance the individuals with low durations of exposures included in the IA 1970 cohort, no excess in cancer incidence is detected;

3) There were a total of 12 out of 47 (26%) members of the Resident Group who reported themselves to have cancer, but, whose diagnosis on follow-up with the Alberta Cancer Registry or with attending physicians, turned out to be a benign lesion (4), an in-situ lesion (3), or could not be confirmed (5);

4) There were no statistically significant deviations between observed and expected number of cancers for sites in the body, other than the anticipated deficit of respiratory cancers (a large proportion of the IA consists of non-smokers);

5) No differences in the age of individuals at the time of diagnosis of their first malignancies were detected;

6) There is little disparity in cancer incidence among the 5 zones defined within the IA (i.e. Mountain View, Hill Spring, Glenwood, Willow Creek and the Pincher Creek region which includes Twin Butte);

7) There is no evidence to suggest that there has been any excess in cancer incidence among residents of the IA during the year 1985.

16. REPRODUCTIVE RISKS AND OUTCOMES

16.1 Sociodemographic Information

To assess the similarity of groups for the analysis of reproductive outcomes, sociodemographic comparisons were prepared for women of child bearing age and women with at least one pregnancy. For the analysis relating to childhood development, sociodemographic comparisons were done for all children under 15 years.

For women who spent at least one year of childbearing age in the areas under study sometime between 1957 and 1985, there is a small shift in the IA women towards the older age group. Also in the primary contrast between IA and SR for women who had at least one pregnancy, there is a slight shift in the IA women towards the older age groups (45-64). For the outmigrant women of childbearing age groups IA(MC) and SR, there is a striking similarity in the age distributions, and the groups are also quite comparable with respect to both religion and to length of residence in their respective areas. For outmigrants with at least one pregnancy, there is no age difference between the IA(MC) and SR groups.

Overall, women in the IA as compared to the SR area are remarkably similar for other variables. The prevalence of non-smokers is only slightly higher in IA and the number of women with post secondary or higher education is somewhat lower in IA. In addition, when contrasting IA and SR to DCCI, one notes the higher prevalences of women who have never used alcohol, smoked, or used oral contraceptives in the IA and SR groups.

When sociodemographic characteristics are analyzed with respect to children and their parents in the study areas, the largest difference noted in the main contrast IA and SR is the difference (13.5%) in the number of mothers who never smoked in

IA. As well, there is a mild shift in the age of the mother at the birth of the child toward the younger age groups in the IA.

When analyzing the pattern of contraceptive use among women in the four areas by decade of birth, there is a similarity across the four study areas. For example, there is a uniform decrease in the prevalence of contraceptive use of women born in the 60's across all four areas, therefore delayed first pregnancy is not commonplace.

All the sociodemographic information suggests that the residents of the areas studied in 1985 are reasonably similar with regard to a large number of key variables. In addition, these residents are very similar to their first degree relatives who left the respective areas with regard to a smaller number of key items (age, religion, length of residence). Outmigrants left the area mostly for education, work or to create a family elsewhere. They left their respective areas at a comparable average age varying between 21.4 and 22.9. This will limit necessarily their reproductive experience in the areas under study.

16.2 Fertility and Fetal Losses

For the proportion of females reporting any fertility problems in the family by age at the time of the problem, there is an approximately 3.2% higher prevalence of such problems in the IA as compared to the SR. However, there is no difference between the prevalence of such reports in DCCI as compared to SR-M.

In analyzing fertility (the number of live births per 1,000 women-years of child bearing age spent in an area) there were no clinically significant differences between the IA and SR.

There is a 3% higher prevalence of reported fetal losses in the IA as compared to the SR. The largest difference found was between SR and IA for the youngest age group. (Table 16.2/3)

16.3 Low Birth Weight

The occurrence of low birth weight (less than 5.5 pounds or 2.5 Kg) is similar in IA and SR (5.0 for each) and the lowest in DCCI (3.8).

16.4 Congenital Anomalies

The prevalence of anomalies observed objectively in physical examination and noted in the judgemental exams or in specialist consultations are both low and similar across all four areas. The rates remain similar when observations are limited to participants born in the areas of comparison.

The crude proportions of deliveries leading to birth defects as reported by participants were slightly different: the IA groups with a prevalence of 6.3% and the SR group with 4.6%.

For the occurrence of major birth defects in IA, SR and DCCI, the numbers observed were compared to the numbers expected using the condition-specific rates measured from the experience of the general population in Manitoba in 1985. The numbers are remarkably similar comparing IA to SR. Table 16.4/3. The deficit in DCCI is noteworthy.

16.5 Childhood Development

Even though IA was somewhat higher than SR no clinically significant differences between areas were found in rates of problems reported by parents. For developmental characteristics measured in the field and for the Denver Developmental Screening Test there were no differences between areas.

TABLE 16.2/3

PROPORTION (%) OF PREGNANCIES LEADING TO REPORTED FETAL LOSSES IN PARTICIPANTS AND OUTMIGRANTS

Age of Mother at Time of Loss	AREA							
	IA		SR		DCCI		SR-M	
	%	N	%	N	%	N	%	N
< 20	17.4	46	3.4	29	0	20	0	11
20-24	11.8	323	12.1	140	17.8	118	18.5	54
25-29	15.4	357	9.5	169	14.0	129	14.3	77
30-34	14.6	192	11.7	128	15.4	52	13.2	53
35-39	13.2	106	18.8	48	14.3	14	10.0	10
40-44	25.5	47	33.3	9	22.2	9	0	6
45-49	33.3	3	33.3	3	0	0	50	2
Combined	**14.5**	**1074**	**11.8**	**526**	**15.1**	**338**	**13.9**	**216**

TABLE 16.4/3

OBSERVED MAJOR BIRTH DEFECTS IN PARTICIPANTS AND OUTMIGRANTS COMPARED TO EXPECTED NUMBERS, BETWEEN 1957 AND 1985

	AREA					
	IA		SR		DCCI	
N	906		466		285	
	OBS.	EXP.*	OBS.	EXP.*	OBS.	EXP.*
Neural tube defects	0	1.0	0	0.5	0	0.3
Hydrocephalus	0	0.6	0	0.3	0	0.2
Cleft lip	1	0.7	1	0.3	0	0.2
Cleft palate	1	0.5	2	0.2	0	0.1
Pyloric stenosis	5	2.1	1	1.1	2	0.7
Hypospadias	2	1.7	1	0.9	0	0.5
Congenital hip dysplasia	7	7.6	1	3.9	0	2.4
Downs syndrome	1	1.4	1	0.7	0	0.4
Anomalies of septal closure	2	4.1	3	2.1	0	1.2
Total	19	19.7	10	10.0	2	6.0
Observed to expected ratio (OER)	0.96		1.00		0.33	
95% confidence interval for OER	0.58 - 1.51		0.48 - 1.84		0.04 - 1.20	

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* Based on rates for each condition in the population of Manitoba in 1985.

17. MORTALITY

17.1 Person-Years of Risk

The person-years of risk used in this analysis are identical to those used in the study of cancer risks and outcomes. The IA 1970 cohort males experienced a total 15,585 person-years of risk during the period 1970-84, while the females experienced a total of 14,590 person-years of risk.

17.2 Expected Deaths

Using similar reference populations as in the cancer study (a Census Division containing the SR and another including DCCI), expected mortalities are calculated for the IA 1970 cohort males (137.9 and 140.2) and for the IA 1970 cohort females (70.0 and 78.6) based on the two reference area rates respectively.

17.3 Standardized Mortality Ratio Analysis

As seen in Table 17.3/1, the observed numbers of deaths and the expected number of deaths are similar. The data yield standardized mortality ratios which are not significantly different from unity. Thus, even with unconfirmed deaths included, these data indicate no overall excess in the mortality experience of the IA 1970 cohort.

17.4 Post-Hoc Sample Size Considerations

Analysis based on post-hoc sample size considerations indicates that the chance of failing to detect a true clinically significant elevation in mortality is very low since the power to detect an SMR of 1.2 is 80% in a two-sided test.

TABLE 17.3/1

STANDARDIZED MORTALITY RATIOS FOR INDEX AREA 1970 COHORT STANDARDIZED TO THE TWO REFERENCE AREAS

Group	Observed Deaths in the Index Area 1970 Cohort	Expected Deaths Based on RA1	Expected Deaths Based on RA
Index Area 1970 Cohort Males	123	137.9	140.2
Index Area 1970 Cohort Females	61	70.0	78.6
Index Area 1970 Cohort Combined	184	207.9	218.8
SMR* (95% CI)		0.88 (0.73, 1.08)	
SMR** (95% CI)			0.84 (0.69, 1.03)

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* Reference Area 1 = Census Division 2 excluding Lethbridge, an area which contains the SR control area.

** Reference Area 2 = Census Division 6 excluding Calgary, an area which contains the DCCI control area.

17.5 Secondary Mortality Analysis

When mortality rates for the entire Alberta general population are used in analysis, the resulting standardized mortality ratios for the IA 1970 cohort for both males and females shows that the cohort has a very favourable mortality compared to the general population of Alberta. With 21 unconfirmed deaths imputed to the cohort, the SMR is 0.74 (an SMR of 1.0 would mean an identical mortality experience). Excluding the 21 unconfirmed deaths, the SMR is 0.66 (0.54, 0.81).

18. DISCUSSION

18.1 Recapitulation of Main Objective

The main general objective of the study was to determine whether the residents of the Index Area experienced adverse health effects more often than is expected from frequencies derived in the most similar unexposed population to the IA in Alberta, which proved to be the Stirling/Raymond (SR) area. For certain phenomena such as mortality and incidence of cancer where the numbers in the SR area would have been too small and too unstable as a useful control, residents of Southern Alberta excluding the main cities, or census subdivisions constructed from subdivisions to simulate the SR as closely as possible were used. For some contrasts, all of Alberta was used. Ancillary comparisons were made with Didsbury, Carstairs, Crossfield, Irricana (DCCI) area and also using subsets of the entire Canadian population.

18.2 Overview of Measures to Minimize Bias and to Enhance Reliability of Data

Methodological results suggest that serious biases were kept to a minimum and that they are unlikely to affect any of the findings for the major pre-selected variables of this study. The following tactics were employed in the various components of the project to minimize bias and to enhance reliability of data:

1) The control areas were meticulously chosen with the most sophisticated geographic and demographic techniques available to insure maximum comparability to IA in this non-experimental design. The principal comparison group to the Index Area, namely the Stirling/Raymond area, was declared in advance to be the main contrast.

2) All data-gathering instruments, questionnaires, and forms for both ritualized and judgemental medical examinations were carefully developed or adapted, tested, and pre-tested in the field, in Montreal. A

final "dress rehearsal" of a survey similar to that conducted in Alberta was done in the Eastern Townships of Quebec near the Town of Waterloo for the purpose of identifying and eliminating most problems related to the structure, sequence, and item content of the data-gathering instruments.

3) Data-gatherers (both interviewers and physicians) and all coders, although aware of the general purpose of the Medical Diagnostic Review (MDR), were neither cognizant of the specific hypotheses of the study nor of the specific intent of any questionnaire or physical examination item employed in the field. This minimized conscious or unconscious interpretation and distortion of observations in the field.

4) The training of all data-gathering staff, including laboratory technicians, could not be lengthy but was very intensive and rigourous. Many checks on the reliability of data-gatherers at all levels were done during training, such as standardized evaluation of clinical findings with use of simulated or standardized patients for physicians, and checks of inter-observer variation during training of pulmonary function technicians. In addition, periodically throughout the summer, the Quebec and Mayo Clinic laboratories analyzed standardized human hair samples of known trace metal concentrations prepared and certified by the National Institute for Environmental Studies in Japan.

5) A 10% sample of laboratory determinations for trace metals were sent to the Mayo Clinic to check the reliability and accuracy of the findings from the Centre de Toxicologie du Quebec. This was done with fully informed consent of both laboratories.

6) Subjective clinical symptoms were elicited in a standardized way without deviation from the probes and questions used, following a standardized questionnaire administered by trained health services research interviewers. A distinct feature of this project was the "ritualized" medical examination in which the physicians observing and measuring physical signs followed a precisely standardized method and sequence of examination and reporting for all findings. These physicians were only allowed to speak to subjects sufficiently to have them do the clinical manoeuvres required. Thus those physicians' opinions were not invoked about physical findings; only physicians' observations, with the highest attainable rigour of quantification possible, were recorded.

In contrast, by design, the judgemental medical examination was not standardized. The senior physicians involved were allowed to function as they normally would in university clinic practice in order not to restrict their ability to diagnose conditions that may have been missed by the other more inflexible data-gathering procedures. Issues of reproducibility were addressed by having each judgemental physician work in each of the comparison areas as far as was possible. However, the data gathering form employed for the judgemental medical examination was standardized.

7) After the clinical co-principal investigators returned to Montreal, they consulted with other medical specialists to develop formal algorithms to identify specific clinical conditions. These algorithms used data from the questionnaire and ritualized examination as well as from physiological and biochemical tests. The data were extracted and combined by means of computer programs to assure the objectivity and repeatability of counting the frequency of conditions and describing the frequency of clinical phenomena.

8) Comparison of electrocardiograms were based only on the computerized interpretations. Thus, we deliberately traded some degree of validity, which may have been decreased by not taking clinical judgement into account, for the reliability and precision of the computerized ECG measures.

9) Selected descriptive variables from the questionnaire were verified independently by a supervisor. This was achieved by re-interviewing approximately 10% of the households by telephone after the interview had been completed.

10) All data that were not self-coding and which required coding by the field staff or the analysis staff in Montreal were double coded in a random sample of 10% of the participants. This was to determine an error rate in coding and to make corrections in the process when necessary.

11) All coding and transformation of data followed pre-tested standard techniques recorded in coding manuals created and adapted in the field. These are on file for reference.

12) The investigators employed the usual method of 100% double entry and verification of data at the time of keypunching.

13) All data gathering in the field was completed in one season for the cross-sectional survey and by mail within an eight month period for outmigrants.

14) Very high response rates were set as the goal initially. The requirements were specified in advance to be at least 90%. Those rates were achieved in all three areas within the time period specified in the protocol.

15) The response rates were similar for the three areas in the cross-sectional survey across the three areas and for the three outmigrant groups.

16) Half of the research team worked in the SR control area in the first half of August 1985 and moved to the DCCI area after August 15, while the half that had started in DCCI moved to the SR area on August 15. Thus the two areas had approximately equal amounts of information elicited by each half of the staff.

17) For certain data that could have been susceptible to variation due to a change in prevalence of pollens and other allergens between June of 1985 to the end of the summer, a repeat of selected findings was done later in August among respondents who had been first evaluated in June. This was to check on any intra-seasonal variation in the findings of relevance.

18) For similar selected variables related mainly to the respiratory system, clinical and laboratory findings were repeated in winter (late January 1986) to determine whether there was inter-seasonal variation. Again, this focussed largely on respiratory clinical findings and respiratory function in the laboratory.

19) The field staff working in the Index Area did half the determinations in the first half of the winter exercise period then moved to the SR area, while those in the SR area moved to the Index Area in the second half. Thus each team elicited information in both areas for the winter exercise.

20) In order to determine whether there was bias due to selective migration of persons in and out of the three areas for health reasons, an exhaustive search of outmigrants was done. These were people who had lived in the area at any time after 1957 and had moved out or died since that time.

21) Outmigrants were sought using multiple sources. Reporting by at least two independent sources was required for an outmigrant to be officially counted as part of the denominators.

22) Clinical significance for differences between the areas contrasted for any self-reported dichotomous variable required that the levels of statistical significance and power employed in the analysis be declared in advance.

23) Until near the end of the analysis period, the analysis of data was done with the Principal Investigator and co-principal investigators largely blind to the identity of the comparison groups contrasted. This minimized conscious or unconscious approaches to the data that might have influenced conclusions in any particular direction.

24) During a major part of the summer, eight simulated or standardized patients were examined by the sequence of clinical and para-clinical determinations in the field to determine whether there were any drifts in performance by the data-gathering staff.

25) All editing of outmigrant information was performed without knowledge of subsequent outcomes such as cancer or untoward reproductive events.

26) When discretionary choices were made regarding editing of outmigrant information, the _a priori_ policy was adopted that the estimate giving rise to lower person-years of risk was used, so as to decrease the expected number of cancers. This policy is liberal in that it increases the likelihood of concluding that there was an excess in the Index Area.

27) Lastly, before official submission of the findings to the Scientific Advisory Board of the Acid Deposition Research Program, all findings were submitted for exhaustive criticism by an international panel of epidemiologists, biostatisticians, clinical investigators, and environmental scientists and chemists (the SAG). One specific mandate to them was to search for any bias which the investigators had not suspected that could either be checked or corrected prior to the public release of the findings.

18.3 Discussion of the Findings Pertaining to the Main Outcomes put Forward in the Protocol of the Medical Diagnostic Review Project

The following are some highlights of this section:

1) In discussion on the cancer study, it was noted that the IA is a rural farming population with a great deal of exposure to the sun and thus an observed excess of non-melanotic skin cancer is not unexpected nor is it statistically significant. An unexpected finding was a

statistically non-significant small excess of cancer of the prostate (compared to expected incidence). Such an excess has also been noted in parts of Southern Alberta before; it is not unique to the IA. (Bako et al, Can J Public Health, 1982:73;92-94.)

2) Previous studies have reported elevated levels of certain trace metals among samples of volunteers in Southwestern Alberta. The levels of trace metals are very low in all three areas, similar among the three and more than 93% of all values for all metals were either undetectably low or normal with both laboratories.

3) It is very difficult to measure and evaluate the potential influence of occupational and environmental exposures on reproductive health. The difficulties are compounded by additional problems such as small sample size, difficulties in quantifying exposure dosage, changes in reproductive patterns with time, differential recollection of reproductive events, potential biases associated with heightened awareness of environmental exposures and the difficulties of validating data medically, especially fetal losses. Also there are many confounding factors to be considered such as the use of alcohol and tobacco, family history, earlier reproductive history and maternal age. Given these serious limitations, it is encouraging to note that self-reported rates for spontaneous fetal loss and for major congenital anomalies at birth in the IA do not exceed those expected on a population basis despite the potential for heightened recall in IA and DCCI areas. In addition, the rates are not materially different from those in the comparison areas. Most importantly, the prevalence of observed abnormalities from birth in physical examinations are the same in IA and SR.

4) When assessing the point prevalence of any chronic irreversible disease in the IA there was no difference between IA and SR self-reported among adults for the chronic irreversible diseases explored except for the prevalence of musculoskeletal ailments of the joints and limbs. Curiously, hips and legs were affected primarily. For musculoskeletal disorders, although this is corroborated in comparisons of DCCI vs. SR-M, musculoskeletal disorders were not hypothesized in advance as a cardinal problem. The investigators are unaware of any biologically plausible mechanism that might explain this, therefore this finding may have resulted either from multiple comparisons as a statistical artifact or selective recall on the part of participants.

5) With the exception of "hypertension with complications" and "chronic bronchitis", delineation or diagnoses using formal algorithms showed little difference for most of the important diseases explored. The differences for hypertension with complications and chronic bronchitis technically do not attain clinical significance by the pre-set criteria. However, the differences are sufficiently high for the investigators to have "tagged" them as worthy of attention in the balance of the analysis.

For the hypertension question, the investigators reanalyzed the data as if the entire MDR project had been done expressly to do screening for hypertension. Thus, although IA reported more hypertension than SR, the ultimate criteria for population problems with hypertension is the mean level of measured blood pressure which was slightly lower in IA as compared to SR. The differences in related paraclinical findings were small.

With respect to chronic bronchitis, contrary to the findings from questionnaires and computer algorithms using subjective reporting, chronic bronchitis was less prevalent both in IA than SR, and IA than DCCI when diagnosed by judgemental physicians. Most importantly, all examinations of pulmonary function using spirometry resulted in similar levels between IA and SR or performance suggesting that IA participants had better function.

6) With respect to cardinal clinical findings, it is noteworthy that the progression from subjective assessments to more objective data results in a switch in the IA vs. SR excess of symptoms to a deficit for signs.

19. CONCLUSIONS

The following is a summary of conclusions reached by the investigators:

1) The mortality experience of the Index Area from 1970 through 1984 is that which would be expected based on reference rates from similar populations in Southern Alberta and considerably more favourable than for Alberta as a whole.

2) There is no evidence to suggest an excess in the overall incidence of cancer in the Index Area. With the exclusion of non-melanotic skin cancers, the data suggest that residents of this area experience a lower than expected overall incidence of the remaining killing and disabling malignancies.

3) Levels of trace metals in hair and blood specimens from people in the Index Area are within normal limits and are not different than those found in specimens taken from similar populations assessed in this study.

4) The distribution of respiratory function of residents of the Index Area is within normal limits and similar to the respiratory function of residents in the reference populations.

5) The prevalence of medically-observed birth defects in the participants of the cross-sectional survey was similar in all areas. The observed rates of the more common major birth defects are similar to the expected rates derived using Manitoba registry information applied to the Southern Alberta population. Moreover, the overall rates of fetal loss and birth defects determined in this study do not exceed expected rates derived in other Canadian and North American jurisdictions under surveillance with registries.

6) Both men and women report slightly higher rates of problems of fertility in the IA compared to the SR area. The differences do not suggest the existence of a health problem in any area we surveyed.

7) Based on objective clinical assessment, the investigators found no excess of delayed or abnormal childhood development among residents of the Index Area and their offspring.

8) From the full array of major health status outcome measurements and indicators the investigators conclude that Index Area residents do not have different prevalences of life-threatening disorders or seriously

disabling disease than the SR area.

9) There are no detectable differences between the rate of objective cardinal signs in the Index Area and the rate in the main reference population.

10) The investigators detected a small excess of some of the symptoms which residents of IA have reported for many years. These are largely the cardinal symptoms. The investigators ascertained heterogeneous complaints which suggest discomfort and sustained distress. The symptoms include burning and watering of eyes, runny nose, itching of the skin, throat irritation, sputum production, tingling and trembling of hands, fatigue, back pain, and leg and hip pain.

11) The differences in the clinical entities recollected and reported by the participants which are systematically higher in IA as compared to SR are not large enough to contradict or cast doubt upon the major outcome findings. The differences do not constitute an important demonstrated health effect, either good or bad, when the rates of the subjective events are somewhat higher or lower in IA than in the reference populations.

    In a population that has been alarmed for more than two decades about the possible adverse effects of environmental contaminants, it is not surprising that individual persons may often emphasize their subjective sensations, and that such sensations may be reported at a rate higher than can be confirmed with objective evidence. The reassurance provided by the objective evidence may be helpful to many individuals in the IA region.

12) Persons migrating out of all three areas tend to be younger and somewhat healthier than those that remain in the geographic areas demarcated for the study. Moreover, the investigators did not find differences in the patterns of either reported illness or health related events among the three groups of outmigrants. The investigators conclude further that the percentage of persons migrating due to health reasons is extremely low, similar among the three areas, and unlikely to have resulted in selective migration that could render invalid the cross-sectional comparisons of the populations living in the Index Area, SR and DCCI in 1985.

13) The findings of this study were not biased by either intraseasonal or interseasonal variation.

14) There is no detectable association between residence in the Index Area (including Twin Butte, Glenwood, Mountain View, Hill Spring and Willow Creek) and levels of measurable health among people who live there now or lived there in the past. Neither is there any suggestion of association between residence in the Didsbury, Carstairs, Crossfield, Irricana area and the health status of the population living there.

15) The frequencies of health-related phenomena measured, including mortality, cancer incidence, abnormalities of reproduction, disease prevalence, levels of cardinal clinical findings, and laboratory tests in DCCI are consistent with the profile of a healthy community with patterns of health indicators similar to those elsewhere in Canada. Most particularly, DCCI is similar in health status to its best-matched reference population (SR-M). These findings are noteworthy because both DCCI and SR-M are sociodemographically representative of people living in rural areas throughout Alberta.

16) There is no clinical, epidemiologic, or statistical reason to evaluate the causal significance of any possible association between residence in the Index Area and compromised health since such an association was not detected. The present study was not designed to determine causation of any effect that might have been observed, but findings taken on the whole do not suggest that there is any causal effect to be investigated.

17) The overall conclusion: The greatest concerns of the population in the Index Area were about excess mortality, high rates of cancer, diminished respiratory function, dangerous levels of trace metals in the body, higher rates of unfavourable reproductive outcomes and birth defects, and delayed or abnormal childhood development. For all the foregoing concerns the investigators have not detected objective evidence to perpetuate the concerns. The investigators are confident of the scientific basis of that reassurance. With respect to symptoms or how people feel concerning possible contamination of their environment, there is a small difference suggesting greater concern and more awareness of one's health and one's sensations among residents in the Index Area. That is entirely understandable and indeed expected given a quarter century of equivocal information about health in relation to the immediate environment which has been diffused in Southern Alberta.

20. RECOMMENDATIONS

20.1 Emission Controls

None of the findings in this study can or should be interpreted as a medical or epidemiological justification to relax continuing efforts of industry and government in the control of potentially hazardous constituents of sour gas emissions and other environmental contaminants. The investigators recommend a sustained policy of strict protection of the environment in Alberta, both in the near term and as a socially responsible long-range plan.

20.2 An Alberta Registry of Birth Defects

To permit valid and reasonably efficient population surveillance or special studies of adverse health events related to reproduction, the investigators recommend that the Province of Alberta promote and fund the upgrading of registration of birth defects. The quality of the resulting Registry of Birth Defects would be similar to the commendable level of quality of the Alberta Cancer Registry. The principles of operation should be mandatory reporting and active surveillance of exposure factors. Its scope should be province-wide. Its system should facilitate inter-provincial comparisons. The initial steps already taken by the University of Calgary in the southern areas of the province should be supported and expanded, with participation of the University of Alberta for full inclusion of northern regions.

20.3 Further Population Health Studies

Any health study in the Index Area will be affected both by the unavoidably low statistical power for detecting small differences or large proportionate differences in uncommon findings, and selective recall of symptoms or health events. This is inherent in the size of the Index Area population and in the nature of the clinical problems and not resolvable by another study and less so by uninformed "private" impressions. The investigators recommend that further clinical, epidemiologic or demographic studies involving new data collection on the field not be done.